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Negative pressure wound therapy for surgical wounds healing by primary closure (Review)

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[Intervention Review]

Negative pressure wound therapy for surgical wounds healing by primary closure

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ABSTRACT

Background

Indications for the use of negative pressure wound therapy (NPWT) are broad and include prophylaxis for surgical site infections (SSIs). While existing evidence for the effectiveness of NPWT remains uncertain, new trials necessitated an updated review of the evidence for the effects of NPWT on postoperative wounds healing by primary closure.

Objectives

To assess the effects of negative pressure wound therapy for preventing surgical site infection in wounds healing through primary closure.

Search methods

We searched the Cochrane Wounds Specialised Register, CENTRAL, Ovid MEDLINE (including In-Process & Other Non-Indexed Citations), Ovid Embase, and EBSCO CINAHL Plus in February 2018. We also searched clinical trials registries for ongoing and unpublished studies, and checked reference lists of relevant included studies as well as reviews, meta-analyses, and health technology reports to identify additional studies. There were no restrictions on language, publication date, or setting.

Selection criteria

We included trials if they allocated participants to treatment randomly and compared NPWT with any other type of wound dressing, or compared one type of NPWT with another type of NPWT.

Data collection and analysis

Four review authors independently assessed trials using predetermined inclusion criteria. We carried out data extraction, 'Risk of bias' assessment using the Cochrane 'Risk of bias' tool, and quality assessment according to GRADE methodology.

Main results

In this second update we added 25 intervention trials, resulting in a total of 30 intervention trials (2957 participants), and two economic studies nested in trials. Surgeries included abdominal and colorectal (n = 5); caesarean section (n = 5); knee or hip arthroplasties (n = 5); groin surgery (n = 5); fractures (n = 5); laparotomy (n = 1); vascular surgery (n = 1); sternotomy (n = 1); breast reduction mammoplasty (n = 1); and mixed (n = 1). In three key domains four studies were at low risk of bias; six studies were at high risk of bias; and 20 studies were at unclear risk of bias. We judged the evidence to be of low or very low certainty for all outcomes, downgrading the level of the evidence on the basis of risk of bias and imprecision.

Primary outcomes

Three studies reported mortality (416 participants; follow-up 30 to 90 days or unspecified). It is uncertain whether NPWT has an impact on risk of death compared with standard dressings (risk ratio (RR) 0.63, 95% confidence interval (CI) 0.25 to 1.56; very low-certainty evidence, downgraded once for serious risk of bias and twice for very serious imprecision).

Twenty-five studies reported on SSI. The evidence from 23 studies (2533 participants; 2547 wounds; follow-up 30 days to 12 months or unspecified) showed that NPWT may reduce the rate of SSIs (RR 0.67, 95% CI 0.53 to 0.85; low-certainty evidence, downgraded twice for very serious risk of bias).

Fourteen studies reported dehiscence. We combined results from 12 studies (1507 wounds; 1475 participants; follow-up 30 days to an average of 113 days or unspecified) that compared NPWT with standard dressings. It is uncertain whether NPWT reduces the risk of wound dehiscence compared with standard dressings (RR 0.80, 95% CI 0.55 to 1.18; very low-certainty evidence, downgraded twice for very serious risk of bias and once for serious imprecision).

Secondary outcomes

We are uncertain whether NPWT increases or decreases reoperation rates when compared with a standard dressing (RR 1.09, 95% CI 0.73 to 1.63; 6 trials; 1021 participants; very low-certainty evidence, downgraded for very serious risk of bias and serious imprecision) or if there is any clinical benefit associated with NPWT for reducing wound-related readmission to hospital within 30 days (RR 0.86, 95% CI 0.47 to 1.57; 7 studies; 1271 participants; very low-certainty evidence, downgraded for very serious risk of bias and serious imprecision). It is also uncertain whether NPWT reduces incidence of seroma compared with standard dressings (RR 0.67, 95% CI 0.45 to 1.00; 6 studies; 568 participants; very low-certainty evidence, downgraded twice for very serious risk of bias and once for serious imprecision). It is uncertain if NPWT reduces or increases the risk of haematoma when compared with a standard dressing (RR 1.05, 95% CI 0.32 to 3.42; 6 trials; 831 participants; very low-certainty evidence, downgraded twice for very serious risk of bias and twice for very serious imprecision. It is uncertain if there is a higher risk of developing blisters when NPWT is compared with a standard dressing (RR 6.64, 95% CI 3.16 to 13.95; 6 studies; 597 participants; very low-certainty evidence, downgraded twice for very serious risk of bias and twice for very serious imprecision).

Quality of life was not reported separately by group but was used in two economic evaluations to calculate quality-adjusted life years (QALYs). There was no clear difference in incremental QALYs for NPWT relative to standard dressing when results from the two trials were combined (mean difference 0.00, 95% CI −0.00 to 0.00; moderate-certainty evidence).

One trial concluded that NPWT may be more cost-effective than standard care, estimating an incremental cost-effectiveness ratio (ICER) value of GBP 20.65 per QALY gained. A second cost-effectiveness study estimated that when compared with standard dressings NPWT was cost saving and improved QALYs. We rated the overall quality of the reports as very good; we did not grade the evidence beyond this as it was based on modelling assumptions.

Authors' conclusions

Despite the addition of 25 trials, results are consistent with our earlier review, with the evidence judged to be of low or very low certainty for all outcomes. Consequently, uncertainty remains about whether NPWT compared with a standard dressing reduces or increases the incidence of important outcomes such as mortality, dehiscence, seroma, or if it increases costs. Given the cost and widespread use of NPWT for SSI prophylaxis, there is an urgent need for larger, well-designed and well-conducted trials to evaluate the effects of newer NPWT products designed for use on clean, closed surgical incisions. Such trials should initially focus on wounds that may be difficult to heal, such as sternal wounds or incisions on obese patients.

PLAIN LANGUAGE SUMMARY

Negative pressure wound therapy for surgical wounds healing by primary closure

Review question

We reviewed the evidence about the effectiveness of negative pressure wound therapy (NPWT) for preventing surgical site infection (SSI).

Background

Surgical site infections are common wound infections that develop at the site of a surgical incision. The incidence of SSI may be as high as 40% for some types of surgery, and may also be higher for people with medical problems such as diabetes or cancer. Surgical site infections increase patient discomfort, length of hospital stay, and treatment costs.

Negative pressure wound therapy involves a sealed wound dressing connected to vacuum pump that sucks up fluid from the wound, which is thought to promote wound healing and prevent infection. In an earlier 2014 version of this review, we found the effectiveness of NPWT to be unclear. This new update includes the results of new trials conducted since that time.

Study characteristics

In February 2018 we searched for randomised controlled trials (studies in which participants are assigned to one of two or more treatment groups using a random method) that compared NPWT with other dressings or with another type of NPWT for the prevention of SSI. We found 25 additional trials, resulting in a total of 30 trials (2957 participants), and two economic studies. The types of surgery included abdominal surgery, caesarean section, joint surgery, and others. The included trials were small, with most recruiting fewer than 100 participants.

Key results

Evidence of low certainty shows that NPWT may reduce the incidence of SSI. We are uncertain if NPWT reduces the incidence of death, dehiscence (reopening of the wound), seroma (excessive fluid under a wound), haematoma (formation of blood clots), readmission to hospital, or repeat surgery. It is uncertain if NPWT results in more dressing-related blisters, or whether the treatment costs more on average than a standard dressing. Results from one trial suggest that NPWT may be more cost-effective than standard care when the impact of an SSI on length of hospital stay and other hospital costs is taken into account.

Quality of the evidence

Most of our results are based on evidence of very low certainty, resulting in a high level of uncertainty in our findings. This was due to a lack of information about the methods used in the trials or a lack of adherence to some of the key standards required for conducting randomised controlled trials. In addition, when a trial involves too few participants, it cannot be accurately assessed if NPWT leads to more benefit or harm. To increase confidence in our results, more high-quality, independently funded trials are needed.

Summary of findings for the main comparison. Negative pressure wound therapy compared with standard dressing for surgical wounds healing by primary closure

Negative pressure wound therapy compared with standard dressing for surgical wounds healing by primary closure

Patient or population: adult patients with surgical wounds healing by primary closure
Setting: general surgical and orthopaedic wards in acute care hospitals
Intervention: negative pressure wound therapy
Comparison: standard dressing

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with standard dressing	Risk with negative pressure wound therapy				
Mortality	Study population		RR 0.63 (0.25 to 1.56)	416 (3 studies)	⊕⊖⊖⊖ Very low[1]	It is uncertain whether NPWT has an impact on the incidence of mortality compared with a standard dressing. Mortality data was reported in only 3 small studies, the low number of deaths contributed to the wide confidence intervals.
	53 per 1000	33 per 1000 (13 to 83)				
Surgical site infection	Study population		RR 0.67 (0.53 to 0.85)	2547 (23 studies)	⊕⊕⊖⊖ Low[2]	NPWT may decrease the incidence of surgical site infection compared with a standard dressing. However, only 3 of the trials included more than 100 participants.
	151 per 1000	96 per 1000 (78 to 119)				
Dehiscence	Study population		RR 0.80 (0.55 to 1.18)	1507 (12 studies)	⊕⊖⊖⊖ Very low[3]	It is uncertain whether NPWT increases or decreases the incidence of dehiscence compared with a standard dressing.
	70 per 1000	56 per 1000 (39 to 80)				
Reoperation	Study population		RR 1.09 (0.73 to 1.63)	1021 (6 studies)	⊕⊖⊖⊖ Very low[3]	It is uncertain whether NPWT increases or decreases the incidence of reoperation compared with a standard dressing.
	83 per 1000	86 per 1000 (58 to 128)				
Readmission	Study population		RR 0.86 (0.47 to 1.57)	1271 (7 studies)	⊕⊖⊖⊖ Very low[3]	It is uncertain whether NPWT increases or decreases the incidence of readmission compared with a standard dressing.
	46 per 1000	43 per 1000				

		(26 to 70)				
Seroma - incidence	Study population		RR 0.67 (0.45 to 1.00)	568 (6 studies)	⊕⊖⊖⊖ Very low[3]	It is uncertain if the incidence of seroma is decreased when NPWT is compared with a standard dressing.
	112 per 1000	75 per 1000 (51 to 112)				
Haematoma	Study population		RR 1.05 (0.32 to 3.42)	831 (6 studies)	⊕⊖⊖⊖ Very low[4]	It is uncertain if the incidence of haematoma is increased or decreased when NPWT is compared with a standard dressing.
	14 per 1000	14 per 1000 (5 to 39)				
Skin blisters	Study population		RR 6.64 (3.16 to 13.95)	597 (6 studies)	⊕⊖⊖⊖ Very low[4]	It is uncertain if there is a higher risk of developing skin blisters when NPWT is compared with a standard dressing.
	20 per 1000	138 per 1000 (66 to 289)				

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; **NPWT:** negative pressure wound therapy; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[1]Downgraded once for risk of bias (unclear allocation concealment and incomplete reporting) and twice for very serious imprecision.
[2]Downgraded two levels for unclear or high risk of bias in the following domains: sequence generation, allocation concealment, blinding of outcome assessor (overall very serious risk of bias).
[3]Downgraded twice for unclear or high risk of bias in the domains sequence generation, allocation concealment, and blinding of outcome assessor (overall very serious risk of bias), and once for serious imprecision.
[4]Downgraded twice for unclear or high risk of bias in the domains sequence generation, allocation concealment, and blinding of outcome assessor, (overall very serious risk of bias) and twice for very serious imprecision.

BACKGROUND

Description of the condition

An estimated 4511 operations per 100,000 population are carried out annually worldwide, equating to one operation each year for every 22 people (Lancet Commission on Global Surgery 2015). This figure is higher in high-income countries. For example, in Australia in 2013/14, there were approximately 2.4 million surgical procedures in a population of 23.4 million, or around one operation each year for every 10 people (ABS 2014). One of the complications of surgery is surgical site infection (SSI), which is an infection that occurs at the site of a surgical incision or in an organ space within 30 days of the surgery. The overall incidence of SSI is 1.9% (Berrios-Torres 2017), but it may be as high as 40% in some populations (Maehara 2017). As well as causing pain and discomfort for the patient, SSI increases the length of hospital stay and the cost of treatment (De Lissovoy 2009).

Surgical wounds generally heal by primary closure during which the wound edges are brought together so that they are adjacent to each other. Wound closure is usually assisted by the use of sutures (stitches), staples, adhesive tape, or glue (Coulthard 2010), and healing begins within hours of closure (Rodero 2010). Some types of surgical wounds, such as sternal wounds, are more difficult to heal due to their anatomical position or an increased likelihood of infection (Toeg 2017); so too are surgical wounds in patients with certain types of underlying characteristics such as advanced age or medical conditions including malnutrition, uncontrolled diabetes, cardiovascular disease, compromised immunity, and morbid obesity (Baronski 2008; Waisbren 2010; Winfield 2016).

Failure of a wound to heal may also be the result of dehiscence (separation of the wound edges). Reasons for dehiscence are either technical, such as sutures breaking, cutting through tissue or knots slipping, or inadequate splinting (Baronski 2008), or patient-related factors such as wound infection and obesity (Sandy-Hodgetts 2015). Chronic obstructive pulmonary disease is a major risk factor for dehiscence in sternal surgery (Olbrecht 2006). The most serious complication of dehiscence is wound evisceration, where the wound separates completely, exposing the underlying organs. Where evisceration occurs, the mortality rate in the postoperative period may be as high as 45% (Kenig 2012).

Description of the intervention

Negative pressure wound therapy (NPWT) has been used to treat wounds since the late 1990s (Fleischmann 1997; Morykwas 1997). Negative pressure wound therapy has been recommended for a diverse range of lesions including open abdominal wounds (Stevens 2009), open fractures (Stannard 2009), burn wounds (Kantak 2016), pressure ulcers (Mandal 2007), post-traumatic wounds (Kanakaris 2007), diabetic foot ulcers (Eneroth 2008), split-thickness skin grafts (Blume 2010), sternal wounds (Sjogren 2011), and after clean surgery in obese patients (Dragu 2011). Negative pressure wound therapy is increasingly being used prophylactically on closed incisional wounds to prevent surgical site complications (De Vries 2016; Webster 2014), as well as being used on wounds healing by secondary intention (left open to heal from the bottom up) such as chronic or infected wounds (Dumville 2015).

Negative pressure wound therapy consists of a closed, sealed system that applies negative pressure (suction) to the wound surface. The wound is covered or packed with an open-cell foam or gauze dressing and sealed with an occlusive drape. Intermittent or continuous suction is maintained by connecting suction tubes from the wound dressing to a vacuum pump and liquid waste collector. Standard negative pressure rates range from −50 mmHg to −125 mmHg (Ubbink 2008; Vikatmaa 2008). The longest-established device is the vacuum-assisted closure (VAC) system (KCI, San Antonio, Texas) (Morykwas 1997). However, alternatives have been developed and are being used (Visser 2017). Portable versions of the device have been introduced for use in community settings (Hurd 2014; Ousey 2014). An emerging advance has been the addition of 'instillations' of sterile water, saline, antiseptics, or antibiotics to VAC therapy, as in new negative pressure wound therapy with instillation (NPWTi) systems such as V.A.C. VeraFlo Therapy (KCI, San Antonio, Texas) (Gabriel 2014; Gupta 2016).

How the intervention might work

In humans, the wound-healing process is regarded as occurring in three consecutive and overlapping stages, namely: inflammation, new tissue formation, and remodelling (Gurtner 2008). The precise way in which NPWT may aid in this process is unclear. Experimental evidence suggests that NPWT may assist wound healing by increasing local blood flow and the production of granulation tissue (Xia 2014), and may encourage other changes to the microenvironment of the wound by reducing bacterial contamination, oedema, and exudate (Banwell 2003). Other mechanisms for healing have been investigated using animal models. For example, an increase in fibrocytes (stem cells involved in wound healing) was demonstrated in an NPWT-treated group of diabetic rats compared with a control group (Chen 2017). Expressions of vascular endothelial growth factor receptors, which are involved in healing, were also seen to increase when NPWT was compared with a control group of rabbits (Tanaka 2016). One of the basic theoretical principles underpinning the development of NPWT is that it increases perfusion or blood flow. However, this was challenged in an experimental study using healthy volunteers that showed that local blood flow decreased as suction pressure increased (Kairinos 2009).

Why it is important to do this review

Surgical wounds that become infected and/or that fail to heal may cause considerable distress to patients and impact negatively on the physical, social, emotional, and economic aspects of their lives (Andersson 2010). Investigations into interventions to avoid wound breakdown are therefore important. Negative pressure wound therapy was approved by the US Food and Drug Administration (FDA) for the treatment of non-healing wounds in 1995 (Kloth 2002). More recently, a multinational expert working group has issued guidelines for the use of the therapy for diabetic foot ulcers, complex leg ulcers, pressure ulcers, dehisced sternal wounds, open abdominal wounds, and traumatic wounds (Expert Working Group 2008). While NPWT has become an accepted part of modern wound-healing techniques, there have also been reports of severe adverse events associated with the therapy. Problems have included stomal dehiscence (Steenvoorde 2009), extraperitoneal bladder leakage (Heuser 2005), necrotising fasciitis (Citak 2010), bleeding after cardiac surgery (Petzina 2010), pain (Apostoli 2008), secondary wound formation (Karabacak 2016), and anxiety (Keskin 2008). Communiqués issued in 2009 by the FDA reported six deaths and 77 injury reports associated with the use of NPWT. The information sheets contained warnings and recommendations for consumers

and healthcare practitioners about the use of the treatment in certain circumstances (FDA 2009a; FDA 2009b).

Since the introduction of NPWT, there has been an explosion of publications (over 2600 in the last 10 years), which have been influential in changing practice. Along with an increase in primary studies and other non-research publications, there has been a concomitant increase in the number of systematic reviews (Hyldig 2016; Ingargiola 2013; Karlakki 2013; Ubbink 2008; Vikatmaa 2008; Willy 2017). Many of these reviews have included non-randomised controlled trials; have considered both acute and chronic wounds; and, as with the primary studies, many have received industry sponsorship (Kairinos 2014). In addition, concerns have been raised about the premature termination of studies (Gregor 2008). It is therefore unsurprising that some recent reviews have concluded that the evidence for the effectiveness of NPWT remains uncertain (Hyldig 2016; Webster 2014; WHO 2016). None of the reviews published to date have included formal cost-effectiveness studies. Negative pressure wound therapy is a rapidly expanding therapy with widening indications for its use, so new trials continue to emerge. Consequently, an updated systematic review was required to summarise the current evidence for the effect of NPWT on the healing of surgical wounds by primary closure.

A glossary of main terms is given in Appendix 1.

OBJECTIVES

To assess the effects of negative pressure wound therapy for preventing surgical site infection in wounds healing through primary closure.

METHODS

Criteria for considering studies for this review

Types of studies

For changes to this section, please see Differences between protocol and review.

We included only randomised controlled trials (RCTs) that evaluated the effects of NPWT on surgical wounds healing by primary closure. This criterion encompassed comparative full and partial economic evaluations conducted within the framework of eligible RCTs (i.e. cost-effectiveness analyses, cost-utility analyses, cost-benefit analyses, and cost analyses). We did not include trials of split-skin grafts, full-skin grafts, flap closure, skin graft donor sites, or wounds that could not be closed immediately due to damaged tissue (e.g. in severe trauma), infection, or chronicity. We also excluded cross-over trials and quasi-randomised studies where, for example, treatment allocation was made through alternation or by date of birth.

Types of participants

We included trials involving people of any age and in any care setting that used NPWT for uninfected surgical wounds healing by primary closure. We excluded trials where NPWT was used as a dressing following a skin graft or where the surgery involved harvesting veins following flap elevation.

Types of interventions

The primary intervention was NPWT delivered by any mode, such as vacuum-assisted (VAC) closure (KCI, San Antonio, Texas) or simple closed-system suction drainage; continuously or intermittently over any time period and at any pressure. The comparison interventions were any standard dressing (e.g. gauze) or any advanced dressing (e.g. hydrogels, alginates, hydrocolloids); or comparisons between different negative pressure devices.

Types of outcome measures

Primary outcomes

- Mortality
- Surgical site infection
- Dehiscence

Secondary outcomes

- Reoperation
- Readmission to hospital within 30 days for a wound-related complication
- Seroma
- Haematoma
- Skin blisters
- Pain (measured by any valid pain assessment instrument)
- Quality of life (measured by any valid assessment instrument and including utility scores representing health-related quality of life)
- Dressing-related costs (including the cost of the dressing and healthcare professional time)
- Resource use (healthcare treatment costs per patient per wound; costs of health practitioner time or visits; costs of hospital stay for wound healing; procedure costs to treat adverse events, infections, or complications; costs of hospital stay resulting from adverse events and complications)
- Quality-adjusted life year gained (QALY)
- Incremental cost-effectiveness ratio (ICER)

Search methods for identification of studies

Electronic searches

We searched the following electronic databases to identify reports of relevant clinical trials:

- the Cochrane Wounds Specialised Register (searched 28 February 2018);
- the Cochrane Central Register of Controlled Trials (CENTRAL; 2018, Issue 1) in the Cochrane Library (searched 28 February 2018);
- Ovid MEDLINE including In-Process & Other Non-Indexed Citations (1946 to 28 February 2018);
- Ovid Embase (1974 to 28 February 2018);
- EBSCO CINAHL Plus (Cumulative Index to Nursing and Allied Health Literature; 1937 to 28 February 2018)

The search strategies for the Cochrane Wounds Specialised Register, CENTRAL, Ovid MEDLINE, Ovid Embase, and EBSCO CINAHL Plus can be found in Appendix 1. We combined the Ovid MEDLINE search with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity-

and precision-maximising version (2008 revision) (Lefebvre 2011). We combined the Embase search with the Ovid Embase filter developed by the UK Cochrane Centre (Lefebvre 2011). We combined the CINAHL searches with the trial filters developed by the Scottish Intercollegiate Guidelines Network (SIGN 2015). There were no restrictions with respect to language, date of publication, or study setting.

We conducted separate searches to identify economic evaluations in the following electronic databases:

- Ovid MEDLINE including In-Process & Other Non-Indexed Citations (1946 to 28 February 2018);
- Ovid Embase (1974 to 28 February 2018);
- EBSCO CINAHL Plus (Cumulative Index to Nursing and Allied Health Literature; 1937 to 28 February 2018);
- NHS Economic Evaluation Database (NHS EED; 2015, Issue 2) in the Cochrane Library (searched 28 February 2018).

We used economic filters developed by the Centre for Reviews and Dissemination in combination with terms to describe the condition and intervention in Ovid MEDLINE, Ovid Embase, and EBSCO CINAHL searches (CRD 2010). There were no restrictions on the above searches with respect to language, date of publication, or study setting.

We also searched the following clinical trials registries on 25 June 2018 (search strategies for clinical trial registries can be found in Appendix 2):

- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (clinicaltrials.gov);
- World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) (apps.who.int/trialsearch/Default.aspx);
- EU Clinical Trials Register (www.clinicaltrialsregister.eu/ctr-search/search);
- Australian and New Zealand Clinical Trials Registry (www.anzctr.org.au).

Searching other resources

We checked the citation lists of papers identified by the above strategies for further reports of eligible studies. We contacted corresponding authors of identified studies. In the first version of this review, we contacted the manufacturers and distributors of devices used to deliver NPWT, such as vacuum-assisted (VAC) closure (KCI, San Antonio, Texas); SNaP Wound Care System Dressing (Spiracur Inc, Sunnyvale, California); Venturi Avanti and Venturi Compact (Talley Group, Romsey, UK); and RENASYS EZ (Smith & Nephew, Hull, UK). We did not contact manufacturers or distributors for this update.

Data collection and analysis

We carried out data collection and analysis according to the methods stated in the published protocol (Webster 2011), which were based on the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

JW and WC were authors of some of the papers included in this review. To prevent any form of bias, neither JW or WC were involved in extracting data or assessing quality for any of the studies in which they were investigators.

Selection of studies

Two review authors independently reviewed titles and abstracts identified by the search. We retrieved full reports of all potentially relevant trials for further assessment of eligibility based on the inclusion criteria. We settled differences of opinion by consensus. There was no blinding of study authorship.

Data extraction and management

Two review authors independently extracted the following data using a predesigned checklist:

- methods (number of participants eligible and randomised, adequacy of randomisation, allocation concealment, blinding, completeness of follow-up);
- participant characteristics and exclusions;
- type of surgery;
- setting;
- study dates;
- interventions;
- number of participants per group;
- prospective registration on a clinical trials registry;
- information about ethics approval, consent, and conflict of interest;
- source of funding;
- economic data (healthcare costs);
- outcomes.

Any discrepancies were resolved through discussion. One review author (JW) entered data into the Review Manager 5 software (Review Manager 2014); MS and WC checked the data for accuracy. Where necessary, we attempted to contact study authors of the original reports for clarification. When more than one publication arose from a study, we extracted data from all relevant publications but did not duplicate data.

Assessment of risk of bias in included studies

Two review authors independently assessed the eligible trials for risk of bias using the Cochrane tool for assessing risk of bias (Higgins 2011). This tool addresses six specific domains, namely sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other potential sources of bias (see Appendix 3 for details of the criteria on which our judgements were based). We assessed blinding and completeness of outcome data for each outcome separately. We completed a 'Risk of bias' table for each eligible study. Any disagreements between review authors were resolved by consensus. We contacted investigators of included trials to resolve any ambiguities. Assessment of risk of bias is presented as a 'Risk of bias' summary figure, which shows all the judgements in a cross-tabulation of study by entry (Figure 1; Figure 2).

Figure 1. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

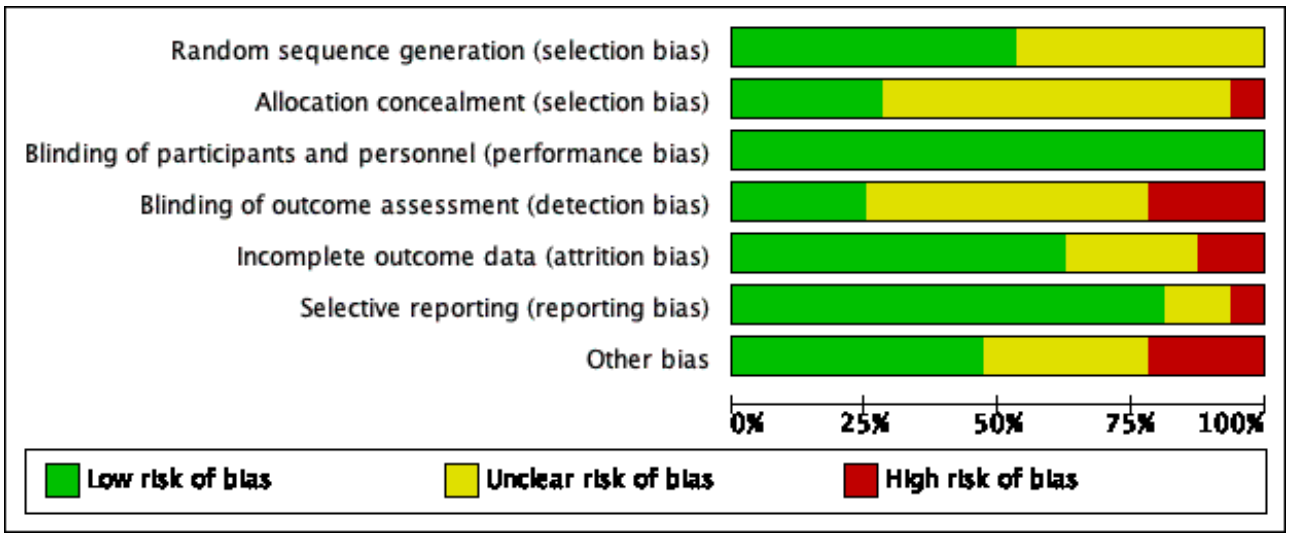


Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

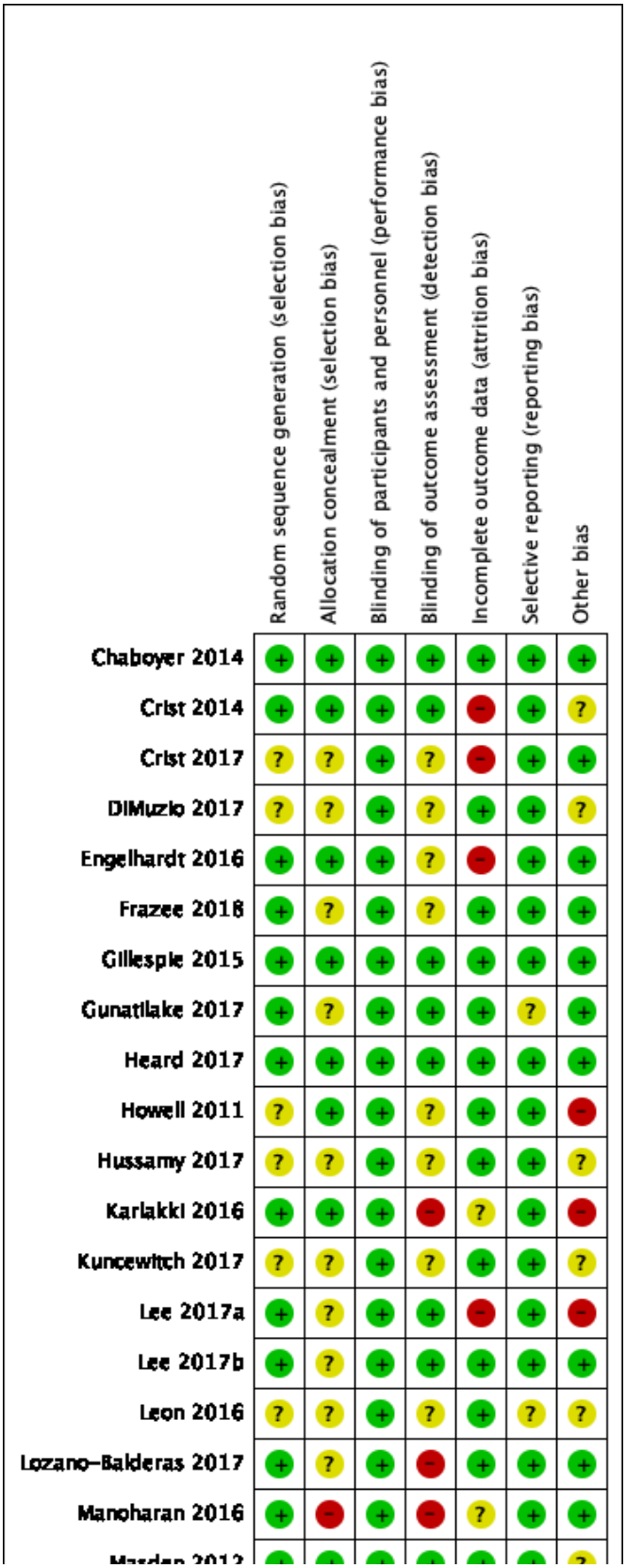
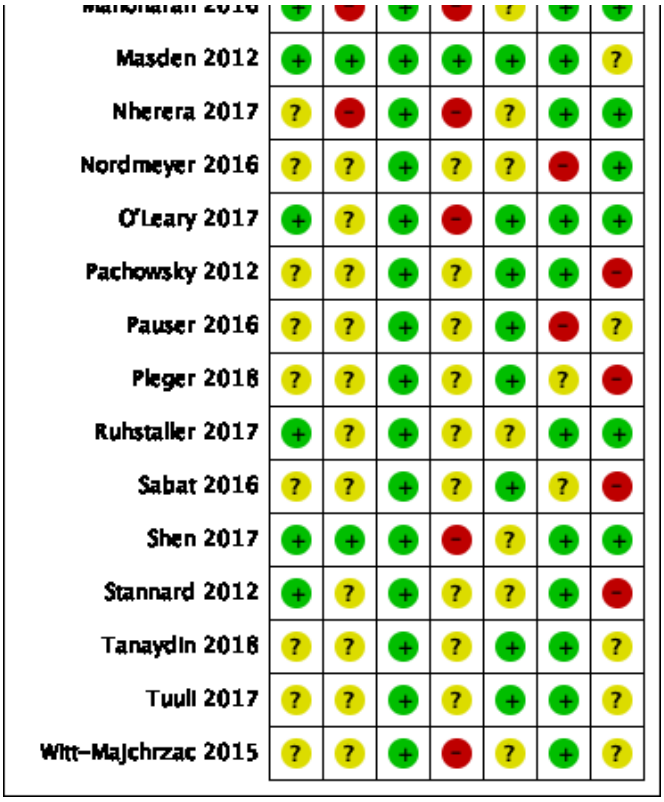


Figure 2. (Continued)



We reported bias, and more generally study limitations within economic evaluations, using the checklist from the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) (Husereau 2013), and used the scoring system reported by Hope 2017 to assess the overall quality of each study, expressed as a percentage. Specifically, we allocated 1 point for each item that was fully met, 1/2 point if the item was partially met, and 0 for each item that was not met. We summed the total score and calculated a percentage (total score/total number of items less any non-applicable (N/A) item). We classified the quality of a report as follows: 85% or higher as excellent; 70% to 84% as very good quality; 55% to 70% as good quality; and below 55% as poor quality.

Measures of treatment effect

For individual trials, we extracted the numbers with an event for each treatment group and used them to calculate the risk ratio (RR) with its 95% confidence interval (CI). For statistically significant effects, we planned to calculate the number needed to treat for an additional beneficial outcome (NNTB) or number needed to treat for an additional harmful outcome (NNTH) from the risk difference. However, based on the quality of the data and lack of evidence of effect for most outcomes, we decided not to conduct these calculations. For continuous outcomes, we extracted the mean and standard deviation (SD) and calculated the mean difference (MD) or, if the scale of measurement differed across trials, the standardised mean difference (SMD), each with its 95% CI.

Economic analyses

We have presented a tabulated analysis of the identified economic data in accordance with current guidance on the use of economics methods in the preparation of Cochrane Reviews (Shemilt 2011). We classified the economic evaluation according to the framework described by Husereau and colleagues (Husereau 2013). We tabulated the main characteristics and results of the identified economic evaluation studies and augmented these with a narrative description. The methods used are discussed, and the key results of the studies compared. We assessed the quality of the studies using the CHEERS checklist (Husereau 2013).

We expected the results of cost-effectiveness studies to vary according to the particular circumstances of each study. For example, the comparator treatment, such as standard care, may differ for different types of wounds and in different settings. Our analysis placed the results of the economic studies in context and entailed a discussion of scenarios that were likely to lead to the most cost-effective use of the therapy, as well as the least cost-effective use.

Costs

We intended to capture and report all substantial costs that were observed to differ between participants administered NPWT and participants administered standard care as part of the economic analysis.

We intended to report unit costs along with the currency and price year in each original study. These costs would then be converted to 2016 values by applying implicit price deflators for gross domestic product (GDP) of that currency and then converted into the currency most frequently observed in the articles reviewed using GDP Purchasing Power Parities (Shemilt 2010). This would permit readers of the review to make meaningful comparisons

between costs in studies that may have been conducted in different countries and at different times.

The main costs were expected to be those associated with the NPWT itself; specialist and other practitioner costs as measured by time or number of visits; potential cost-savings from a change in the number of bed days in hospital; and costs stemming from differing rates of adverse events and complications (including procedures initiated due to the failure of wounds to heal, such as amputation). The key cost drivers were identified from the included studies. This enables users of the review to gain a clear understanding of the nature of resource use associated with NPWT.

Outcomes

The primary trial outcome (adverse events) is relevant to the economic analysis as it may indicate a difference in the number of hospital bed days and specialist time required and a possible improvement in quality of life of the participant.

We examined information on the change in health-related quality of life via utilities measured by a multi-attribute utility instrument (MAUI) or other approaches (such as the time trade-off, standard gamble) where possible. These data would ideally be reported in trials for both the group treated with NPWT and a control group receiving the comparator wound care. We assessed the utility data for comparability and representativeness considering issues such as the types of wounds included, the patient populations, timing of the baseline point and follow-up collection, the MAUI used, and the algorithm for scoring the MAUI. We planned to discuss the potential impact on health-related quality of life attributable to the intervention as part of the analysis.

If differences were observed in the rates of adverse events, wound infections, and complications resulting from the treatment of the wound, we planned to discuss the economic implications as part of the economic analysis.

Unit of analysis issues

Where studies randomised wounds or body parts as opposed to individuals and we were unable to obtain further information from trialists, we presented narrative summaries of the results. We excluded cross-over trials.

We also included studies with the split-body design where either people with two similar burn wounds were enrolled and each burn wound was randomised to one of the interventions, or where one half of a wound was randomised to one treatment and the other half to a different treatment. These approaches are similar to the 'split-mouth' approach (Lesaffre 2009). These studies should be analysed using paired data which reflects the reduced variation in evaluating different treatments on the same person. However, it was often unclear whether such an analysis had been undertaken. We have noted this lack of clarity in the 'Risk of bias' assessment and in the notes in the Characteristics of included studies table.

Dealing with missing data

Where it appeared that data had been excluded from the analyses, we attempted to contact authors for these missing data. If data remained missing despite our best efforts to obtain them, we conducted an available-case analysis, based on the numbers of participants for whom outcome data were known. In one case where the SD was missing, we used a validated imputation method and imputed the SD from the another trial that had similar results (Furukawa 2006). No other imputations were made. We did not conduct planned best-case and worst-case analyses, nor did we calculate SDs from standard errors (SE) using the formula SD = SE x $\sqrt{}$N (Higgins 2011).

Assessment of heterogeneity

Assessment of heterogeneity can be a complex, multifaceted process. Firstly, we considered clinical and methodological heterogeneity, that is the degree to which the included studies varied in terms of participant, intervention, outcome, and characteristics such as length of follow-up. This assessment of clinical and methodological heterogeneity was supplemented by information regarding statistical heterogeneity, assessed using the Chi^2 test (we considered a significance level of $P < 0.10$ to indicate statistically significant heterogeneity) in conjunction with the I^2 statistic (Higgins 2003). The I^2 examines the percentage of total variation across RCTs that is due to heterogeneity rather than chance (Higgins 2003). In general, I^2 values of 40% or less may not be important (Higgins 2003), while values of more than 75% or more indicate considerable heterogeneity (Deeks 2011). However, these figures are only a guide, and it has been recognised that statistical tests and metrics may miss important heterogeneity. Thus, while these were assessed, the overall assessment of heterogeneity assessed these measures in combination with the methodological and clinical assessment of heterogeneity. Where there was evidence of high heterogeneity we attempted to explore this further; see Data synthesis for details on how we handled potential heterogeneity in the data analyses.

Assessment of reporting biases

We assessed selective outcome reporting for each trial as part of our appraisal of risk of bias. In addition, as 11 trials were included for one of our primary outcomes (surgical site infection), we also assessed publication bias using a funnel plot (Higgins 2011).

Data synthesis

Where studies were clinically similar and outcome measurements comparable, we pooled results using a random-effects model and reported the pooled estimate together with its 95% CI. Where statistical synthesis of data from more than one study was not possible or considered inappropriate, we conducted a narrative review of eligible studies.

We were unable to pre specify the amount of clinical, methodological, and statistical heterogeneity in the included studies, thus we used a random-effects approach for meta-analysis. Conducting meta-analysis with a fixed-effect model in the presence of even minor heterogeneity may provide overly narrow confidence intervals. We would only have used a fixed-effect approach when clinical and methodological heterogeneity was assessed as minimal, and the assumption that a single underlying treatment effect was being estimated held. Chi^2 and I^2 were used to quantify heterogeneity but were not used to guide the choice of a model for meta-analysis. We would have exercised caution when meta-analysed data were at risk of small-study effects because in such a case use of a random-effects model may be unsuitable. In this case, or where there were other reasons to question the selection of a fixed-effect or random-effects model, we planned to assess the impact of the approach using sensitivity analyses to compare

results from alternate models, but this was not implemented (Thompson 1999).

We presented data using forest plots where possible. For dichotomous outcomes, we presented the summary estimate as an RR with 95% CI. Where continuous outcomes were measured, we presented an MD with 95% CI; we planned to pool SMD estimates where studies measured the same outcome using different methods. For time-to-event data, we planned to plot (and if appropriate to pool) estimates of hazard ratios and 95% CIs as presented in the study reports using the generic inverse-variance method in Review Manager 5 (Review Manager 2014). In future updates, where time-to-healing is analysed as a continuous measure but it is not clear if all wounds healed, we will document use of the outcome in the study but will not summarise data or use them in any meta-analysis.

Subgroup analysis and investigation of heterogeneity

Investigations of heterogeneity were not required as inconsistency was low for all outcomes, nor did we consider any population, intervention, or comparator subanalyses to be appropriate. Studies were small and evidence rated as of low to very low certainty, so any subanalysis may have led to misleading findings (Deeks 2011).

We planned a range of subgroup analyses in the protocol for this review, including type of setting, type of device, type of surgery, and type of comparison dressing. Based on the current interest in NPWT as a treatment for wounds healing by primary intention, and given the available data, we have conducted one of these suggested analyses: a subgroup analysis for different types of surgery is presented in Analysis 1.2, defined in line with broad clinical grouping. This was a post hoc decision resulting in an exploratory analysis and, as with all subgroup analysis, the results should be interpreted with caution.

Sensitivity analysis

We performed a sensitivity analysis on the primary outcomes of surgical site infection to assess the influence of removing studies classified as being at high risk of bias from the meta-analysis. We excluded studies that were assessed as having high or unclear risk of bias in the key domains of adequate generation of the randomisation sequence, adequate allocation concealment, and blinding of outcome assessor. We planned to conduct this sensitivity analysis for the primary outcome of dehiscence but only two studies would have remained in such an analysis so it was not undertaken.

'Summary of findings' tables and GRADE assessment of the certainty of the evidence

We have presented the main outcomes of the review in a 'Summary of findings' (SoF) table. This table presents key information concerning the quality of the evidence, the magnitude of the effects of the interventions examined, and the sum of available data for the main outcomes (Schünemann 2011a). 'Summary of findings' tables also include an overall grading of the evidence related to each of the primary outcomes, using the GRADE approach. The GRADE approach defines the certainty of a body of evidence as the extent to which one can be confident that an estimate of effect or association is close to the true quantity of specific interest. The quality of a body of evidence involves consideration of within-trial risk of bias, directness of evidence, heterogeneity, precision of effect estimates, and risk of publication bias (Schünemann 2011b). We had planned to create a separate SoF table for each comparison evaluated, but we have included only one comparison in our review. We have presented the following outcomes in the SoF table associated with the comparison of NPWT versus standard care:

- incidence of mortality;
- incidence of surgical site infection;
- incidence of dehiscence;
- Incidence of reoperation;
- incidence of readmission to hospital within 30 days (for wound-related complication);
- incidence of seroma;
- incidence of haematoma;
- incidence of skin blisters.

Where data were not pooled, or where outcomes exceeded the recommended seven important outcomes, we conducted a GRADE assessment for each of these outcomes and presented these assessments in a narrative format within the Results section, without presenting them in separate 'Summary of findings' tables.

RESULTS

Description of studies

See Characteristics of included studies; Characteristics of excluded studies; Characteristics of studies awaiting classification; Characteristics of ongoing studies.

Results of the search

We searched for both intervention studies and economic evaluations for this update. The results of these searches are reported separately below together with the changes to the review, and are shown in Figure 3.

Figure 3. Study flow diagram.

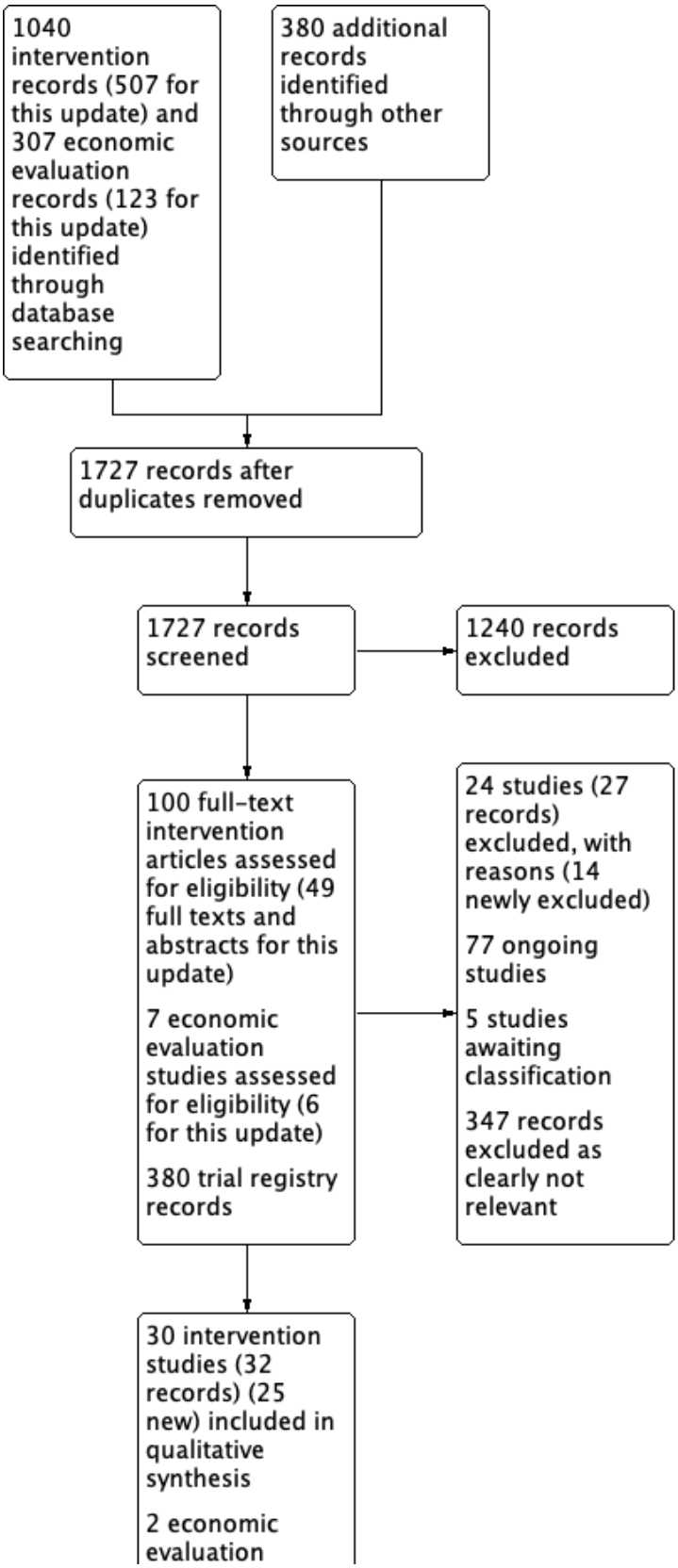
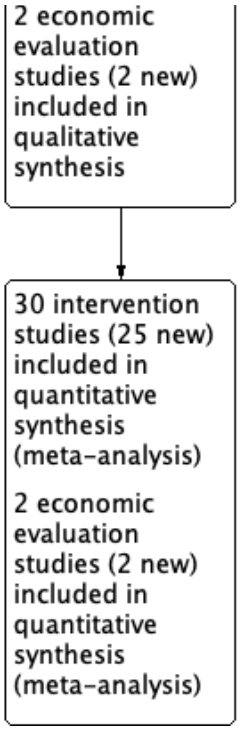


Figure 3. (Continued)



Over the lifetime of the review we have assessed a total of 1040 records as abstracts for intervention studies and 100 at full text. We have assessed 307 records as abstracts and seven as full texts for the economic evaluation studies. We have also identified a total of 380 records from trial registries, resulting (by an iterative process) in 75 records classified as relating to currently ongoing trials (a further two were identified from intervention searches), and five that are awaiting classification.

Interventions search

For this second update, we identified 507 unique new records through our electronic search. We retrieved 49 publications for inspection (42 full-text papers and 7 published abstracts). From these, we selected 25 new intervention studies reported in 27 records for inclusion in the review.

This second update includes 30 intervention studies (Chaboyer 2014; Crist 2017; DiMuzio 2017; Engelhardt 2016; Frazee 2018; Gillespie 2015; Gunatilake 2017; Hussamy 2017; Karlakki 2016; Kuncewitch 2017; Lee 2017a; Lee 2017b; Leon 2016; Lozano-Balderas 2017; Manoharan 2016; Nordmeyer 2016; O'Leary 2017; Pauser 2016; Pleger 2018; Ruhstaller 2017; Sabat 2016; Shen 2017; Tanaydin 2018; Tuuli 2017; Witt-Majchrzac 2015). Seven of these studies were reported in abstract form only.

The previous update of this review included nine studies (Chio 2010; Crist 2014; Dorafshar 2012; Howell 2011; Llanos 2006; Masden 2012; Pachowsky 2012; Petkar 2012; Stannard 2012). We excluded four studies from previous versions of the review: in three studies the 185 participants underwent skin grafts, so no longer met our inclusion criteria (Chio 2010; Llanos 2006; Petkar 2012), and in the fourth trial (Dorafshar 2012; 87 participants), NPWT was used on existing wounds of mixed origin, and separate data for surgical wounds could not be obtained.

We sought additional information from the corresponding authors of the following new trials: Gillespie 2015; Karlakki 2016; Manoharan 2016; Nordmeyer 2016; Pauser 2016; Ruhstaller 2017; Shen 2017; Tuuli 2017; Witt-Majchrzac 2015. We received responses providing additional useful information from only two authors (Gillespie 2015; Shen 2017).

Trial registries search

In previous versions of this review, a search of trial registry platforms identified 37 protocols related to NPWT. The investigator of one protocol stated that the planned start date for the trial was early 2011 (ACTRN12609000995279). We have been unable to find any further information about this study, so it has been removed from the studies awaiting classification. In the first version of the review, we sent emails to all the manufacturers mentioned in our search strategy. We were advised of one animal study, but identified no further human studies meeting our inclusion criteria, and did not contact manufacturers for this second update.

For the current version of the review, the clinical trials registry search identified 343 records (see Appendix 2 for details). We did not contact investigators from these trials, nor did we analyse the trials' status.

- ClinicalTrials.gov (searches completed 25 June 2018)
- WHO ICTRP (searches completed 25 June 2018)

Screening by two review authors identified 75 ongoing studies and five studies awaiting classification from these records. We have categorised two studies from the main searches as ongoing studies giving a total of 77 ongoing studies.

Economic analysis search

Electronic searches for previous versions of the review yielded 184 references, none of which met our economic inclusion criteria. For this update, we identified a further 123 publications, six of which were retrieved for full-text examination. We included two in the review (Heard 2017; Nherera 2017), both of which were based on trials included in this review: Chaboyer 2014 and Karlakki 2016, respectively.

One of the studies from an earlier search initially appeared to be relevant (Mullins 2012). This was an abstract from a conference presentation, but we were unable to extract sufficient information from the abstract to include the study in the review. A full report of the study has still not been published, and attempts to contact the author have been unsuccessful, so we have removed the reference from studies awaiting classification.

Included studies

Types of participants

In this update we included 25 additional intervention studies enrolling 2473 participants with 2545 wounds (Chaboyer 2014; Crist 2017; DiMuzio 2017; Engelhardt 2016; Frazee 2018; Gillespie 2015; Gunatilake 2017; Hussamy 2017; Karlakki 2016; Kuncewitch 2017; Lee 2017a; Lee 2017b; Leon 2016; Lozano-Balderas 2017; Manoharan 2016; Nordmeyer 2016; O'Leary 2017; Pauser 2016; Pleger 2018; Ruhstaller 2017; Sabat 2016; Shen 2017; Tanaydin 2018; Tuuli 2017; Witt-Majchrzac 2015). The review now includes 2957 participants. All trials had small sample sizes (range 19 to 441), with the majority (23 out of 30 included studies) enrolling fewer than 100 participants.

Participants in five studies had abdominal or colorectal surgery (Frazee 2018; Kuncewitch 2017; Leon 2016; Lozano-Balderas 2017 Shen 2017). Five studies enrolled obese women undergoing caesarean section (Chaboyer 2014; Gunatilake 2017; Hussamy 2017; Ruhstaller 2017; Tuuli 2017). Five studies enrolled people undergoing knee or hip arthroplasties (Gillespie 2015; Howell 2011; Karlakki 2016; Manoharan 2016; Pachowsky 2012). Five studies enrolled people undergoing groin surgery (DiMuzio 2017; Engelhardt 2016; Lee 2017b; Pleger 2018; Sabat 2016). Participants in five studies had fractures (Crist 2014; Crist 2017; Nordmeyer 2016; Pauser 2016; Stannard 2012). In the Masden 2012 study, the target group included mixed wound types; O'Leary 2017 recruited laparotomy patients; Lee 2017a enrolled people undergoing vascular surgery; Witt-Majchrzac 2015 enrolled people with sternotomy wounds; and participants in the Tanaydin 2018 study underwent bilateral superomedial pedicle Wise-pattern breast reduction mammoplasty.

Twelve studies were conducted in the USA (Crist 2014; Crist 2017; DiMuzio 2017; Frazee 2018; Gunatilake 2017; Howell 2011; Hussamy 2017; Masden 2012; Ruhstaller 2017; Shen 2017; Stannard 2012; Tuuli 2017); five in Germany (Engelhardt 2016; Nordmeyer 2016; Pachowsky 2012; Pauser 2016; Pleger 2018); three in Australia (Chaboyer 2014; Gillespie 2015; Manoharan 2016); two in Canada (Lee 2017a; Lee 2017b); one in the UK (Karlakki 2016); one in Ireland (O'Leary 2017); one in Spain (Leon 2016); one in Mexico (Lozano-Balderas 2017); one in Poland (Witt-Majchrzac 2015); one in the Netherlands (Tanaydin 2018); one in Israel (Sabat 2016); and in one the country where the study was conducted was not reported (Kuncewitch 2017).

Types of interventions

Five studies compared the vacuum-assisted closure (VAC) negative pressure device (KCI, San Antonio, Texas), set to −125 mmHg with a standard dressing (Crist 2014; Crist 2017; Howell 2011; Masden 2012; Stannard 2012). The comparison standard dressings varied among the studies: Crist 2014, Crist 2017, and Stannard 2012 described the comparison dressing as "standard gauze"; Howell 2011 used a sterile gauze dressing secured with a perforated, stretchable cloth tape; Masden 2012 described the control dressing as a "non-adhesive silicone layer" (Mepitel; Mölnlycke Health Care AB, Gothenburg, Sweden) and a "bacteriostatic single silver layer" (Acticoat; Smith & Nephew, Hull, UK). Lozano-Balderas 2017 also compared the VAC and described the control as"subcutaneous tissue was approximated with polyglycolic acid and polypropylene was used for the skin".

Engelhardt 2016 compared closed-incision negative pressure therapy (ciNPT) with an absorbent adhesive dressing. Gunatilake 2017 also compared ciNPT, but with Steri-Strips (3M Health Care, ½ inch, St Paul, Minnesota), sterile gauze, and Tegaderm transparent film dressings (3M Health Care Ltd, Loughborough, UK)). Hussamy 2017 compared ciNPT with standard surgical dressing, and Pleger 2018 compared ciNPT (PREVENA Therapy; KCI, San Antonio, Texas) with conventional therapy.

Manoharan 2016, Pachowsky 2012, Pauser 2016, and Ruhstaller 2017 used the PREVENA system and a conventional dry wound dressing as the control treatment. The remaining studies used a PICO (Smith & Nephew, Hull, UK) (Chaboyer 2014; Gillespie 2015; Karlakki 2016; Nordmeyer 2016; O'Leary 2017; Tuuli 2017; Witt-Majchrzac 2015). The comparison dressing in the Chaboyer 2014 and Gillespie 2015 studies was Comfeel (Coloplast, Notting Hill, Australia); in the Karlakki 2016 trial either Mepore (Mölnlycke Health Care AB, Gothenburg, Sweden) or Tegaderm was used as a control; Nordmeyer 2016 used a dry dressing; O'Leary 2017 described the comparison dressing as "a transparent waterproof dressing" (Smith & Nephew, Hull, UK); the comparison dressing used by Tuuli 2017 was Primapore (Smith & Nephew, Hull, UK); and Witt-Majchrzac 2015 described their control dressing as "a conventional dressing".

DiMuzio 2017, Lee 2017a, and Lee 2017b compared NPWT with gauze dressing without providing further details. Kuncewitch 2017 compared the NPWT with "standard surgical dressing", and Leon 2016 compared the NPWT with "usual dressing". Tanaydin 2018 compared a single-use NPWT system with fixation strips (Steri-Strips). Shen 2017 developed a non-commercial negative pressure device using the hospital's central aspiration system at a pressure of −125 mmHg to achieve a vacuum; the comparison dressing was a "standard surgical dressing".

Types of economic outcomes

Three economic outcomes were reported. A cost-effectiveness comparison between NPWT and standard care was available in two studies. Both provided resource use costs, one in Australian dollars, Heard 2017, and one in British pounds (Nherera 2017). Both studies also estimated the quality-adjusted life year gained (QALY). A QALY is a generic measure of disease burden including both the quality and the quantity of life lived (NICE 2013; NICE 2018), and can be used in combination with cost data to assess the value for money of medical interventions (NICE 2013). One QALY equates to one year in perfect health and a year of less than perfect health is worth

less than one, while death is considered to be worth zero (Heard 2017). The estimated incremental cost-effectiveness ratio (ICER) considers the mean cost per QALY, and was only calculated in the Heard 2017 study. Both Heard 2017 and Nherera 2017 were based on trials included in this review: Chaboyer 2014 and Karlakki 2016, respectively.

For further details, see Table 1.

Excluded studies

We have excluded a total of 24 studies, of which eight were newly identified and excluded; four previously included (see above); 10 that were excluded in the first update of this review; and two that were previously awaiting classification.

We excluded five studies in the first version of this review (Hu 2009; Johannesson 2008; Kim 2007; Mouës 2004; Mouës 2007). The intervention dressing in one study was not a negative pressure device (Johannesson 2008); one study was not an RCT (Kim 2007); and three studies did not include acute wounds (Hu 2009; Mouës 2004; Mouës 2007). Two trials assessed as awaiting classification were excluded, as no further information about these studies was available (Braakenburg 2006; Moisidis 2004). In the first update we excluded a further five studies: Albert 2012 (no acute wounds); Banasiewicz 2013 (included participants with infected wounds); Bondokji 2011 (prospective cohort study); Eisenhardt 2012 (none of our outcomes of interest were reported); and Grauhan 2013 (quasi-randomised by time of operation).

In this second update we excluded a further eight trials: two were not RCTs (Li 2016; Pellino 2014), and one study included acute and chronic wounds and results were not reported separately (Rahmanian-Schwarz 2012). In Al-Inany 2002, the intervention evaluated was not NPWT, and in the Visser 2017 trial the vacuum was created by inserting a 25-gauge needle attached to a 10-millilitre syringe subcutaneously into the dressing and aspirating the air; we believed that this technique differed considerably from the other studies and so this study was excluded. Chiang 2017 and Yu 2017 included wounds that were not strictly primarily closed wounds. Anderson 2014 was a feasibility study and was not designed to assess any outcomes relevant to this review. The Eisenhardt 2012 trial included only people with skin grafts and so did not meet our inclusion criteria.

Ongoing studies

We classified two studies from the main searches that were trial protocols as ongoing studies (Nguyen 2017; SUNRRISE 2017), along with 75 from the searches of trial registries.

Risk of bias in included studies

Two studies met our criteria for low risk of bias in each domain (Appendix 3) (Chaboyer 2014; Gillespie 2015), while all of the remaining studies were at high or unclear risk of bias in at least one domain.

Four studies (Chaboyer 2014; Crist 2014; Gillespie 2015; Masden 2012) were at low risk of bias for one or more of 'sequence generation', 'allocation concealment', or 'blinding of the outcome assessor' while six were at high risk for one or more of these (Karlakki 2016; Lozano-Balderas 2017; Manoharan 2016; O'Leary 2017; Shen 2017; Witt-Majchrzac 2015). The remaining 20 studies were at unclear risk of bias for one or more of these domains.

See Figure 1 and Figure 2 for the 'Risk of bias' summary. Risk of bias, or more specifically study quality, for the economic studies is shown in Table 2.

Allocation

Sequence generation

Fifteen of the 30 studies described the use of an adequate process to generate the random allocation list, such as a computer-based random-number generator or a web-based random-number generator (Chaboyer 2014; Crist 2014; Engelhardt 2016; Frazee 2018; Gillespie 2015; Gunatilake 2017; Lee 2017a; Lee 2017b; Lozano-Balderas 2017; Manoharan 2016; Masden 2012; O'Leary 2017; Ruhstaller 2017; Shen 2017; Stannard 2012). Karlakki 2016 used a block size of 20 shuffled envelopes, so no sequence generation was required. The other studies did not specify how the sequence was generated and were assessed as being at unclear risk of bias for this domain (Crist 2017; DiMuzio 2017; Howell 2011; Hussamy 2017; Kuncewitch 2017; Leon 2016; Nordmeyer 2016; Pachowsky 2012; Pauser 2016; Pleger 2018; Sabat 2016; Tanaydin 2018; Tuuli 2017; Witt-Majchrzac 2015).

Allocation concealment

We judged seven of the 30 studies as at low risk of bias for allocation concealment. Two studies used a web-based randomiser to conceal allocation until the point of randomisation (Chaboyer 2014; Masden 2012). Five studies used opaque, sealed envelopes (Crist 2014; Engelhardt 2016; Gillespie 2015; Howell 2011; Karlakki 2016). Surgeons in the Shen 2017 trial were sent an email on the day before surgery advising them of which arm the participants had been assigned to.

The method used for allocation concealment was unclear in 21 studies (Crist 2017; DiMuzio 2017; Frazee 2018; Gunatilake 2017; Hussamy 2017; Kuncewitch 2017; Lee 2017a; Lee 2017b; Leon 2016; Lozano-Balderas 2017; Nordmeyer 2016; O'Leary 2017; Pachowsky 2012; Pauser 2016; Pleger 2018; Ruhstaller 2017; Sabat 2016; Stannard 2012; Tanaydin 2018; Tuuli 2017; Witt-Majchrzac 2015).

Surgeons were notified on the day of surgery before the commencement of the procedure in Manoharan 2016, therefore we judged this study as being at high risk of bias for this domain.

Blinding

Participants and personnel

The appearance of dressings was dissimilar in all of the trials, so blinding was impossible. However, we considered that this would not have affected outcomes, and therefore have rated the trials as at low risk of bias for this domain.

Outcome assessment

Outcome assessors were unaware of group allocation in seven studies, therefore these studies were assessed as at low risk of bias (Chaboyer 2014; Crist 2014; Gillespie 2015; Gunatilake 2017; Lee 2017a; Lee 2017b; Masden 2012).

In six studies outcome assessors, usually surgeons, were not blinded (Karlakki 2016; Lozano-Balderas 2017; Manoharan 2016; O'Leary 2017; Shen 2017; Witt-Majchrzac 2015), and so these studies were assessed as at high risk of bias for this domain.

It was unclear whether the outcome assessor was blinded in the remaining 18 studies.

Incomplete outcome data

We assessed 19 studies as at low risk of attrition bias (Chaboyer 2014; DiMuzio 2017; Frazee 2018; Gillespie 2015; Gunatilake 2017; Howell 2011; Hussamy 2017; Kuncewitch 2017; Lee 2017b; Leon 2016; Lozano-Balderas 2017; Masden 2012; O'Leary 2017; Pachowsky 2012; Pauser 2016; Pleger 2018; Sabat 2016; Tanaydin 2018; Tuuli 2017).

We assessed seven studies as being at unclear risk of attrition bias. In Karlakki 2016 unequal numbers of attrition were reported; the number analysed in each group was not reported in Manoharan 2016 and Nordmeyer 2016; and in Ruhstaller 2017 results were available for 91% of participants in the intervention group and 84% of those in the control group, but it was unclear from the abstract if reasons for loss of follow-up were similar across groups. In the Shen 2017 study, a high proportion of participants were lost from both groups (approximately 30%), and although reasons for losses were similar between groups, it is unclear if outcomes could have been affected by such a high attrition rate. We also assessed Stannard 2012 and Witt-Majchrzac 2015 as at unclear risk of attrition bias where there were no losses from either arm of the study, despite long follow-up periods. In the Stannard 2012 study, a total of 249 patients were recruited from four hospitals. Results were reported for all participants at hospital discharge and also at long-term follow-up (follow-up period not defined). Since four hospitals were involved in this study, it seems unlikely that complete follow-up would have occurred for all of those recruited, which suggests an 'available-case' analysis. Similarly, in the Witt-Majchrzac 2015 trial, there was no attrition at the six-week follow-up visit in either group.

We assessed the remaining four trials as at high risk for attrition bias (Crist 2014; Crist 2017; Engelhardt 2016; Lee 2017a).

Selective reporting

We judged 24 studies to be at low risk of reporting bias, as the trial report suggested that all outcome data collected were reported. All of the reported outcomes were appropriate and expected in this type of study, so we graded these studies as at low risk of reporting bias (Chaboyer 2014; Crist 2014; Crist 2017; DiMuzio 2017; Engelhardt 2016; Frazee 2018; Gillespie 2015; Howell 2011; Hussamy 2017; Karlakki 2016; Kuncewitch 2017; Lee 2017a; Lee 2017b; Lozano-Balderas 2017; Manoharan 2016; Masden 2012; O'Leary 2017; Pachowsky 2012; Ruhstaller 2017; Shen 2017; Stannard 2012; Tanaydin 2018; Tuuli 2017; Witt-Majchrzac 2015). Among them three studies were retrospectively registered, so there was potential for study characteristics to have changed before or during the study (Manoharan 2016; O'Leary 2017; Stannard 2012). Even so, the reported outcomes were consistent with the proposals and appropriate for interventions aimed at reducing SSI, so we also rated these studies as at low risk for reporting bias. In five studies (Howell 2011; Karlakki 2016; Masden 2012; Pachowsky 2012; Witt-Majchrzac 2015), each of the prespecified outcomes as defined in the methods section of the papers was reported in the results, but no published protocol was available. The reported outcomes for these studies were also appropriate, and so these studies were rated as at low risk for reporting bias.

We assessed the Nordmeyer 2016 and Pauser 2016 studies as at high risk of bias for this domain. The two studies were from the same group of researchers, and participants in both studies underwent orthopaedic surgery. Surgical site infection was not reported; the only outcome assessed was seroma.

We assessed the remaining four studies as at unclear risk of bias (Gunatilake 2017; Leon 2016; Pleger 2018; Sabat 2016).

Other potential sources of bias

One of the studies contained unequal numbers in each study arm and was stopped early due to an unacceptably higher rate of blisters among participants in the NPWT group (Howell 2011). In the Pauser 2016 study, outcomes for the NPWT group were reported at day 5 and day 10, but outcomes for the control group were only reported overall; it was unclear what time frame was meant by "overall". A layer of silver was included as part of the "standard dressing" in the Masden 2012 study; it is unclear how this may have affected outcomes. In the Stannard 2012 study, individual participants were randomised, but some participants had more than one wound. The analysis did not account for a clustering effect, creating the possibility of a unit of analysis error. We have presented data from this study separately. In the Karlakki 2016 study, intervention participants were seen in a wound clinic at first week and control participants were not. In the Lee 2017a study, there was high loss to follow-up without reasonable explanation. Pachowsky 2012 was supported by a company, and the decision to publish trial results was made between study authors and study sponsors. There is a potential unit of analysis issue in the Pleger 2018 and Sabat 2016 studies.

Risk of bias in economic studies

See Table 2.

We used the CHEERS checklist, Husereau 2013, to assess the quality of the reports of the two included economic studies (Heard 2017; Nherera 2017). Both studies scored > 80% on the checklist, indicating very good reporting quality. However, the lead author in the Nherera 2017 study was an employee of Smith & Nephew, which manufactures the intervention product used in the study. Additionally, data for the Nherera 2017 study were drawn from the Karlakki 2016 trial, which was at high risk for detection bias. The two items that were least well addressed were 'Measurement and valuation of preference based outcomes' and 'Choice of model'.

Effects of interventions

See: **Summary of findings for the main comparison** Negative pressure wound therapy compared with standard dressing for surgical wounds healing by primary closure

See Summary of findings for the main comparison for the main comparison: NPWT compared with standard dressing for surgical wounds healing by primary closure.

Comparison 1: NPWT compared with standard dressing (30 trials, 2957 participants)

All of the studies in this comparison compared a negative pressure device with a standard dressing. The included surgery types were diverse: study devices varied by manufacturer, and standard dressings differed based on individual hospital preference.

Primary outcomes

Mortality (follow-up period 30 days to 90 days or unspecified)

Three studies (416 participants) reported on this outcome. It is uncertain whether NPWT has an impact on the risk of death compared with standard dressings (risk ratio (RR) 0.63, 95% confidence interval (CI) 0.25 to 1.56) (Analysis 1.1). We classified the evidence as of very low certainty, downgrading one level for serious risk of bias (unclear allocation concealment and incomplete reporting) and twice for very serious imprecision. Although outcome assessments were not blinded we regard this as less important for this outcome and a further downgrade could not have altered the GRADE judgement of certainty which is already very low.

Surgical site infection (follow-up period 30 days to 12 months or unspecified)

Twenty-five studies reported on this outcome.

We pooled incident SSI data from 23 studies (2533 participants; 2547 wounds). The evidence showed that NPWT may reduce the incidence of SSI (NPWT 124/1279 (9.8%) versus standard dressing 191/1268 (14.8%); RR 0.67, 95% CI 0.53 to 0.85) (Analysis 1.2). We judged the evidence as of low certainty, downgrading two levels for very serious risk of bias in the following domains: sequence generation, allocation concealment, and blinding of outcome assessor.

When we applied our sensitivity analysis criteria to include only the four studies at low risk of bias (329 participants) which together found the effect of NPWT on the incidence of SSI to be unclear (RR 0.83, 95% CI 0.47 to 1.46) (low certainty evidence, downgraded twice for very serious imprecision (low numbers of events) although the trials were well-conducted). The evidence remains of low certainty overall whether or not trials at high and unclear risk of bias in important domains are considered in the analysis.

Two studies randomised wounds rather than individuals. Stannard 2012 reported results for this outcome including 249 participants who had sustained open fractures, requiring surgery for closure. Randomisation was by individual participant, but some participants had multiple wounds. Outcome data were collected and analysed by wound, not participant, so we have not carried out further analysis as clustering was not taken into account in this study. The investigators reported that there were 14/144 (9.7%) SSIs in the NPWT group compared with 23/122 (18.9%) SSIs in the standard dressing group. We rated the evidence from this study as of very low certainty, downgrading twice for very serious risk of bias in a number of domains (selection bias, detection bias, attrition bias) and once for serious imprecision. Pleger 2018 randomised 100 participants with 129 groin wounds, and outcome data were collected and analysed by groin wound. The investigators reported that there were 1/58 (1.7%) SSIs in the NPWT group compared with 10/71 (14.1%) SSIs in the standard dressing group. We rated the evidence from this study as of very low certainty, downgrading twice for very serious risk of bias in a number of domains (selection bias and other bias) and once for serious imprecision.

Subgroup analyses

Of the prespecified subgroup analyses, we were only able to conduct the comparison based on different types of surgery. The results of this analysis are shown in Analysis 1.2. There was no evidence of a difference between these subgroups (test for subgroup differences P = 0.13).

Dehiscence (follow-up period 30 days to an average of 113 days or unspecified)

Fourteen studies reported on this outcome.

We combined results from 12 studies (1507 wounds; 1475 participants) that compared NPWT with standard dressings. It is uncertain whether NPWT reduces risk of wound dehiscence compared with standard dressings (RR 0.80, 95% CI 0.55 to 1.18) (Analysis 1.3). We classified this evidence as very low certainty, downgrading three levels: twice for very serious risk of bias in several domains (sequence generation, allocation concealment, and blinding of outcome assessor) and once for serious imprecision. One of these 12 studies reported dehiscence, but these wounds (breasts) were randomised and served as own control (Tanaydin 2018); this study assessed dehiscence in participants who underwent bilateral breast reduction mammoplasty. This was a 'split-body' or 'intra-individual' design where a person with two wounds had one wound randomised to each treatment. It was not clear whether the analysis took this into account.

Two studies reported dehiscence, but these two studies randomised wounds as opposed to individuals. Stannard 2012 assessed dehiscence in participants with an open fracture requiring surgical closure. Participants were randomised individually, but more that one wound per participant was included in the results. We did not have individual patient data, and the trial investigators did not account for clustering in their analysis, so further analysis was not undertaken (NPWT 12/139 (8.6%) versus standard dressing 20/122 (16.4%); very low-certainty evidence, downgraded two levels for very serious risk of bias in several domains (selection bias, detection bias, and attrition bias) and one level for serious imprecision). Pleger 2018 randomised 100 participants with 129 groin wounds, and outcome data were collected and analysed by groin wound. There were 3/58 (5.2%) superficial dehiscences in the NPWT group compared with 4/71 (5.6%) in the standard dressing group, and 1/58 (1.7%) deep wound dehiscences with fat necrosis in the NPWT group compared with 4/71 (5.6%) in the standard dressing group. We rated the evidence from this study as of very low certainty, downgrading twice for very serious risk of bias in a number of domains (selection bias and other bias) and once for serious imprecision.

Secondary outcomes

Reoperation (follow-up period 30 days to an average of 113 days or unspecified)

We assessed the evidence from six trials (1021 participants) on the incidence of reoperation as of very low certainty. It is uncertain if NPWT increases or decreases the number of instances of reoperation when compared with a standard dressing (RR 1.09, 95% CI 0.73 to 1.63) (Analysis 1.4). We downgraded the evidence three levels: twice for unclear or high risk of bias in several domains (sequence generation, allocation concealment, blinding of outcome assessor) and once for imprecision.

Wound-related readmission to hospital within 30 days (follow-up period 10 days to 90 days)

We are uncertain if there is any clinical benefit associated with NPWT for reducing wound-related readmission to hospital within

30 days (RR 0.86, 95% CI 0.47 to 1.57; 7 studies; 1271 participants; very low-certainty evidence, downgraded twice for unclear or high risk of bias in several domains (sequence generation, allocation concealment, blinding of outcome assessor) and once for imprecision) (Analysis 1.5).

Seroma (follow-up period 10 days to 6 weeks)

Seroma was reported in the following three ways.

Firstly, by incidence: it is uncertain whether NPWT reduces risk of seroma compared with standard dressings (RR 0.67, 95% CI 0.45 to 1.00; 6 studies; 568 participants; very low-certainty evidence, downgraded twice for very serious risk of bias in several domains and once for serious imprecision) (Analysis 1.6). Pleger 2018, randomising 100 participants with 129 groin wounds, also reported this outcome: there were 0/58 seroma in the NPWT group compared with 1/71 in the standard dressing group. We rated the evidence from this study as of very low certainty, downgrading twice for very serious risk of bias in a number of domains (selection bias and other bias) and twice for very serious imprecision.

Secondly, by volume on day 10: it remains uncertain if NPWT reduces seroma volume compared with a standard dressings due to very low-certainty evidence (mean difference (MD) -1.70, 95% CI −3.32 to −0.08; 2 studies; 39 participants; very low-certainty evidence downgraded twice for very serious risk of bias and twice for very serious imprecision) (Analysis 1.7).

Thirdly, by volume in cubic centimetre: MD −3.74, 95% CI −6.88 to −0.60; 1 study; 21 participants; very low-certainty evidence downgraded twice for very serious risk of bias and twice for very serious imprecision (Analysis 1.8). We are therefore uncertain if NPWT reduces seroma volume compared with standard dressings.

Haematoma (follow-up period 30 days to 6 weeks)

We pooled incident data from six trials (831 participants). There was no clear difference between groups when NPWT was compared with a standard dressing (RR 1.05, 95% CI 0.32 to 3.42). We rated the evidence as of very low certainty, downgrading twice for very serious imprecision and twice for very serious risk of bias (Analysis 1.9). Pleger 2018, randomising 100 participants with 129 groin wounds, also reported this outcome: there were 0/58 haematoma in the NPWT group compared with 8/71 in the standard dressing group. We rated the evidence from this study as of very low certainty, downgrading twice for very serious risk of bias in a number of domains (selection bias and other bias) and twice for very serious imprecision.

Skin blisters (follow-up period 6 weeks to 12 months)

It is uncertain if there is a higher risk of developing skin blisters when NPWT is compared with a standard dressing (RR 6.64, 95% CI 3.16 to 13.95) (Analysis 1.10). We rated the combined evidence from six studies (597 participants) as of very low certainty, downgrading twice due to several studies being at very serious risk of bias in a number of key domains. We also downgraded twice for very serious imprecision because studies were small and underpowered with very wide confidence intervals.

Pain

Four studies (380 participants) reported pain, but the data could not be pooled. Results from two of the studies reported "no difference" in pain. One study reported a lower pain level in the NPWT group (NPWT median = 0, interquartile range = 0 to 1; standard dressing median = 1, interquartile range = 0 to 3; P = 0.02). Another study reported that there were significantly fewer participants in the NPWT group with less incisional pain both at rest (39/46 (84.8%) versus 20/46 (43.5%); P < 0.001) and with incisional pressure (42/46 (91.3%) versus 25/46 (54.3%); P < 0.001), compared with standard care. We rated the evidence as of very low certainty, downgrading twice for very serious risk of bias and twice for very serious imprecision, therefore we are uncertain whether use of NPWT results in lower pain levels relative to a standard dressing.

Quality of life

Although two studies measured quality of life, results were not reported in their primary reports. Instead, quality of life scores were used to calculate quality-adjusted life years (QALYs) in subsequent cost-effectiveness analyses (see below).

Dressing-related costs (assessed over 6 weeks)

It is uncertain if dressing costs are higher when NPWT is compared with standard care. One study found a per-day cost increase of AUD 35 when NPWT was compared with standard care (MD AUD 35.39, 95% CI 30.87 to 39.91). A second study, where costs were averaged over the episode of care, saw an increase of over AUD 200 in the NPWT group compared with standard care (MD AUD 215.43, 95% CI 185.37 to 245.49). We graded the evidence as overall of very low certainty, downgrading once for serious risk of bias and twice for very serious imprecision with very wide confidence intervals around the effect size (Analysis 1.11).

Economic outcomes

Resource use

Two studies included a formal cost-effectiveness analysis as part of their intervention (Chaboyer 2014; Karlakki 2016); both were pilot studies with small sample sizes. Chaboyer 2014 included obese women undergoing caesarean section (n = 70), and participants in the Karlakki 2016 study were those scheduled for routine knee or hip arthroplasties (n = 220). The first cost-effectiveness analysis, Heard 2017, was based on Chaboyer 2014, and assessed resources in AUD at 2014 values. Data on costs were based on dressing costs, nursing time, length of hospital stay, and postdischarge costs (readmission, visits to healthcare professionals, and medications). The second study, Nherera 2017, was based on Karlakki 2016, and derived costs from standard cost references for the NPWT device from the UK National Drug Tariff and an assumption that each patient used two NPWT dressings. Inpatient care was based on the average of National Health Service reference costs for knee and hip arthroplasties, which, it was assumed, included the cost of the standard care dressing and nursing time. Costs associated with routine postdischarge care were not included because these costs would be similar across groups. Finally, for those who experienced a complication, an assumption was made that they had two general practitioner visits and received one prescription of antibiotics. Resource use was valued in GBP at 2015/16 values (Nherera 2017). We converted Australian dollars to pounds sterling using the tool for converting and standardising currencies recommended for Cochrane Reviews (CCEMG 2016). The conversion rate was 0.48777 pounds sterling to one Australian dollar. Heard 2017 reported additional costs of AUD 133 (GBP 65) for NPWT over standard dressings, whereas Nherera 2017 reported cost savings of GBP 1132 for NPWT compared with standard dressings. When resource use was compared between NPWT and standard care, results were

uncertain (MD GBP 63.04, 95% CI −31.50 to 157.59; low-certainty evidence, downgraded once for serious risk of bias (selection bias, blinding of outcome assessment, and attrition bias) and twice for very serious imprecision due to very wide confidence intervals that cross the line of no effect) (Analysis 1.12).

Quality-adjusted life year (QALY)

Both economic studies reported health-related quality of life. Heard 2017 calculated QALYs using the 12-item Short Form Health Survey (SF-12) version 2, scored with the UK preference-based algorithm (Brazier 2004), while Nherera 2017 used the 36-item Short Form Health Survey (SF-36) with a regression-based scoring algorithm developed from a sample of Jewish Israelis sampled between 1993 and 1994 (Shmueli 1999). The QALYs for both studies were very low: 0.067 (standard deviation (SD) 0.01) in Heard 2017 versus 0.116 (SD 0.01) in Nherera 2017. No SDs were provided for the Nherera 2017 study, so we imputed the SD from the Heard 2017 study. There was no clear difference in incremental QALYs for NPWT relative to standard dressing when results from the two trials were combined (MD 0.00, 95% CI −0.00 to 0.00; moderate-certainty evidence, downgraded once for serious risk of bias) (Analysis 1.13).

Incremental cost-effectiveness ratio (ICER)

Heard 2017 concluded that NPWT may be cost-effective relative to standard care, estimating an ICER value of GBP 20.65 per QALY gained. Based on deterministic results, Nherera 2017 estimated that NPWT was dominant over standard dressings, as NPWT was cost-saving and improved QALYs. Using the CHEERS checklist, we rated the overall quality of the reports as very good, but the studies used different modelling assumptions. Results therefore depend on which resources are incorporated into the model, and on the cost-effectiveness threshold used. We were unable to make a GRADE assessment because the outcome was based on modelling.

DISCUSSION

Summary of main results

Wound complications

The aim of this systematic review was to examine the evidence from RCTs that focused on the effects of NPWT to prevent SSI following acute surgery. We added 25 additional RCTs to this second update, bringing the total number to 30 (2957 participants), and we also added two cost-effectiveness studies (Heard 2017; Nherera 2017). Although NPWT is widely used for a range of surgical applications (Krug 2011), all of the results in this review were assessed as of low or very low certainty. Consequently, the effectiveness of NPWT compared with standard dressings remains unclear for all the outcomes reported in this review, although we found that NPWT *may* reduce the incidence of SSI (low-certainty evidence). A sensitivity analysis that only included trials at low risk of bias in key domains also found low-certainty evidence for a reduction in the incidence of SSI, which was downgraded twice for imprecision. Although a large number of participants have been treated in RCTs of NPWT, the majority of them were enrolled in trials with unclear or high risk of bias in key domains. This is reflected in the results of our GRADE assessments.

We found low-certainty evidence suggesting that when compared with standard dressings, NPWT may be effective in reducing the rate of SSI. It is uncertain whether NPWT reduces risk of death, wound dehiscence, reoperation, readmission to hospital within 30 days, seroma, haematoma, and skin blisters (very low-certainty evidence).

Cost

We found that the average cost for the standard dressing was lower in both trials that assessed this outcome when compared with the NPWT dressing (Gillespie 2015; Manoharan 2016). Although these cost data come from only two trials, additional studies are unlikely to change this finding, unless equipment costs from the manufacturers of NPWT devices are substantially reduced.

Economic outcomes

Two economic studies, Heard 2017; Nherera 2017, based on results from two RCTs, Chaboyer 2014; Karlakki 2016, compared the cost-effectiveness of NPWT with standard dressings. The absolute cost of NPWT was 6 to 12 times greater than that of standard dressings. However, Heard 2017 reported that total costs for the episode of care were higher with NPWT than with standard dressings, whereas Nherera 2017 reported modest cost savings from NPWT. Both economic studies reported small gains in health-related quality of life. Overall, the value for money from NPWT was relatively low in the Heard 2017 study, but NPWT was a dominant strategy in Nherera 2017. The measurement of costs was reasonable in both studies. The measurement of health states, using the SF-12 version 2 in Heard 2017 and the SF-36 in Nherera 2017, was also reasonable. However, the approach to scoring the SF-36 in Nherera 2017, which used a non-preferenced based algorithm developed in the 1990s, is questionable, especially since the SF-6D, a preference-based scoring algorithm for the SF-36 with country-specific weights for the UK (Kharroubi 2007), the USA (Craig 2013), and other countries, is available. Without using a preference-based scoring system, the gains in QALYs estimated by Nherera 2017 may have been over- or understated. All cost-effectiveness estimates should be interpreted in the context of the certainty of the clinical evidence base. In the case of NPWT in primary closure of surgical wounds, this is judged to be low or very low.

Overall completeness and applicability of evidence

Indications for the use of NPWT following surgery are broadening (Acosta 2017; DeCarbo 2010; Pellino 2015; Webb 2017), with a range of new systems on the market, including those designed for use on closed, clean wounds (Allen 2011; Gabriel 2014; Gupta 2016). Studies eligible for inclusion in our review represented abdominal and colorectal patients (n = 5); caesarean section patients (n = 5); knee or hip arthroplasties patients (n = 5); groin surgery patients (n = 5); fractures patients (n = 5); laparotomy patients (n = 1); vascular surgery patients (n = 1); sternotomy surgery patients (n = 1); breast reduction mammoplasty patients (n = 1); and mixed wounds patients (n = 1).

Studies in some types of surgery, such as vascular surgery and chest surgery, were either not included or were under-represented in this review (Acosta 2017). There were no studies involving children and only two small studies included obese patients, who have higher rates of surgical site infection (Althumairi 2016). Trials were small, with the largest enrolling 441 participants; the average number of participants among the other studies was 87. The magnitude of the negative pressure applied varied between trials and it is unclear whether different pressures produce different outcomes. Animal studies indicate that performance is similar across the range of pressures used in the included trials (Morykwas 2001). Another

limitation in the studies was the variation in durations of follow-up , which ranged from the 10th postoperative day, Manoharan 2016; Pachowsky 2012; Pauser 2016, to 12 months after surgery (Howell 2011). Finally, the included studies were geographically limited, as all were from higher income countries: 12 were conducted in the USA, five in Germany, three in Australia, two in Canada, one in the UK, one in Ireland, one in Spain, one in Mexico, one in Poland, one in the Netherlands, one in Israel, and one did not report where it was conducted. This further restricts the external validity of results.

Quality of the evidence

The certainty of the evidence is low or very low, due to risk of bias, small sample size, and wide confidence intervals that included both an effect and no effect or even a harm of the intervention.

Limitations in study design and implementation

We assessed risk of bias according to six domains: sequence generation, allocation concealment, blinding, selective outcome reporting, incomplete follow-up, and other potential biases. Our assessments of the risk of bias for a number of these domains found that all but two of the included studies, Chaboyer 2014; Gillespie 2015, showed limitations in study design and implementation or reporting of these, which have been reported elsewhere in the review (Figure 2). We had particular concern, where blinding of the intervention is difficult or impossible, that there was subsequent uncertainty about allocation concealment and blinding of outcome assessment. Accordingly, we judged the certainty of the evidence to be low to very low for all outcomes. The other limitation was the involvement of industry in at least 14 (where reported) of the 30 included trials. Authors from the Karlakki 2013 trial disclosed conflicts of interest, with all benefiting from funding from the manufacturer of the NPWT device. There continues to be a concern with the issue of manufacturer sponsorship in studies of healthcare products. For example, a review of the effect of manufacturer involvement on studies of NPWT examined 24 studies where 19 had manufacturer involvement. Importantly, 18 of the 19 manufacturer-funded studies showed a positive effect for the manufacturer's product, while one was "impartial" (Kairinos 2014).

Indirectness of evidence

There was no indirectness, as the participants, interventions, and outcomes in the included studies were within the scope of the published review protocol.

Unexplained heterogeneity or inconsistency of results

Statistical heterogeneity was low for all of the outcomes we assessed and, although there was clinical heterogeneity, we do not believe that this impacted on our results. There was also a lack of conformity in the methods, with negative pressure devices, control dressings, and length of follow-up varying between studies. All of the studies were too small to investigate whether NPWT would reduce SSI rates. For example, Gillespie 2016 estimated that 2009 participants would be required to test for differences in SSI rates among obese women requiring a caesarean section. In this review, the average size of studies investigating the effect of NPWT on this population was 99.

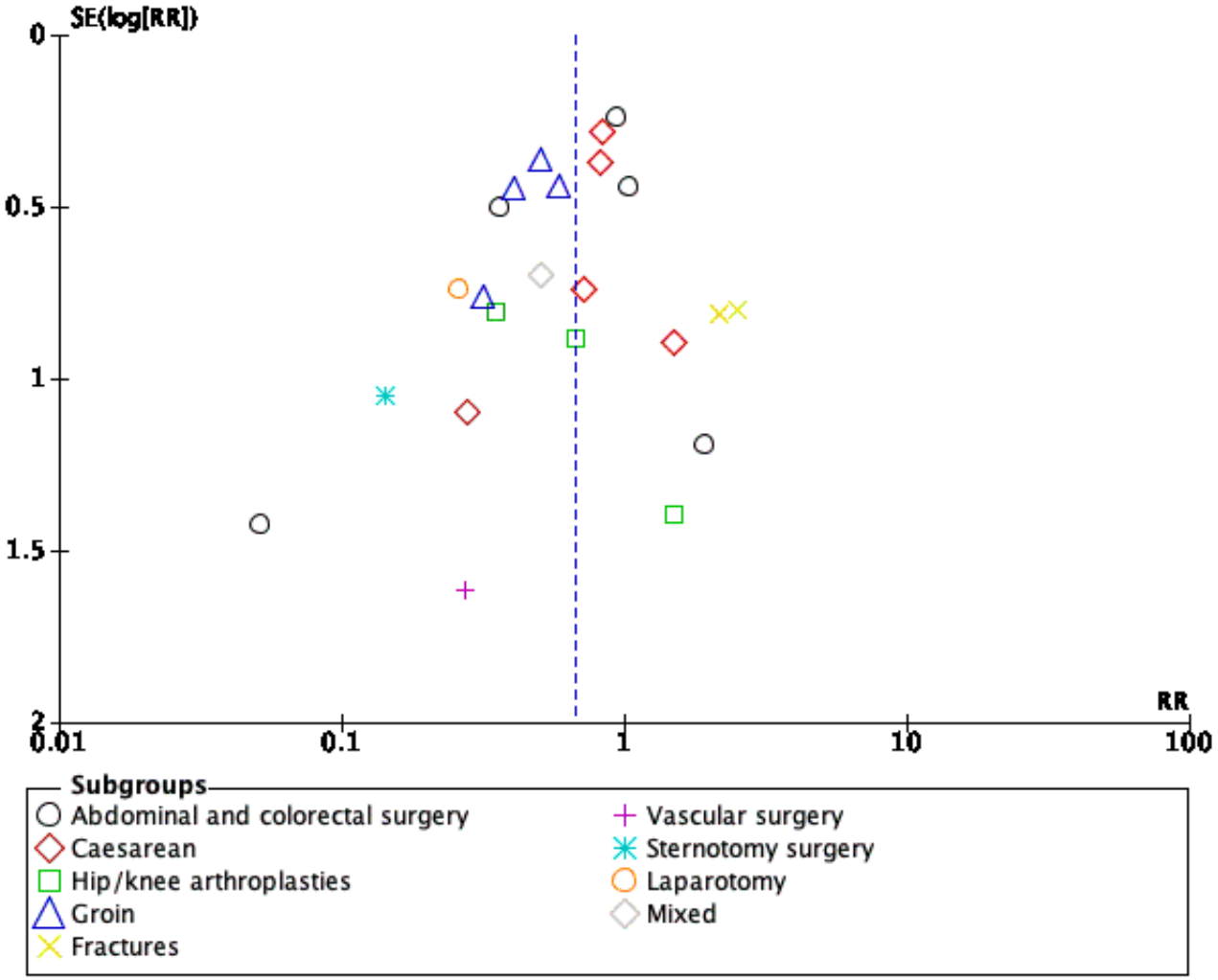
Imprecision of results

Confidence intervals were wide in all of the pooled outcomes, with most crossing 1, indicating uncertainty about whether NPWT was associated with an increase or reduction in outcomes. The imprecision was due to studies being small and underpowered, therefore future, adequately powered studies are likely to have an impact on the certainty of these results.

Publication bias

We feel confident that our comprehensive electronic searches identified all existing, published RCTs addressing the review question, helping to limit bias in the review process. However, a large number of studies (77 ongoing trials) identified primarily through a search of the clinical trial registries have not been published, and we were unable to find any information about them. Moreover, the scant contribution of the 32 included studies, in the face of such wide use of NPWT, is unusual. These two factors may or may not indicate publication bias, but we did not downgrade the evidence for this possibility. The funnel plot (Figure 4) includes all published studies that reported on SSI, but a failure to include results from any unpublished studies may have affected the plot's relative symmetry.

Figure 4. Funnel plot of comparison: 1 Negative pressure wound therapy versus standard dressing, outcome: 1.2 Surgical site infection.



Potential biases in the review process

Clearly described procedures were followed to prevent potential bias in the review process. We conducted a careful literature search, and the methods we used were transparent and reproducible. It is possible that studies published in journals that were outside our search strategy may have been missed. We attempted to contact nine authors, but only two responded. Consequently, we may have underestimated the quality of some studies, simply because their publications did not include the information we required to assess study quality. We have already mentioned our concern about commercial funding, which may have influenced the results of our review. Three of the authors of this review (Webster, Chaboyer, and Scuffham) were also investigators of studies included in the review (Chaboyer 2014; Gillespie 2015; Heard 2017). We were careful to ensure that the trials in which we were involved were critically appraised and that the data were extracted by others. None of the authors of this review has any conflicts of interest or associations with manufacturers of products included in the review. Differences between the published protocol, previous versions of this review (Webster 2011), and the methods used for this update have been described, and a rationale provided in the Differences between protocol and review section.

One study adopted an intra-individual (split-body) approach analogous to the 'split-mouth' design (Lesaffre 2009). This study has particular issues and, if incorrectly analysed, can produce inaccurate confidence intervals around the estimates of effect.

Agreements and disagreements with other studies or reviews

One early systematic review of NPWT included chronic and acute wounds and was published before seven of our included trials were undertaken (Ubbink 2008); it also included an earlier trial that we excluded from our review (Moisidis 2004), so results are not comparable. Our findings also differ from those of two other systematic reviews that evaluated the effectiveness of NPWT for incisional wounds. Important differences in the inclusion criteria account for the differences: the first review included 10 RCTs and five observational studies (Ingargiola 2013), and the second review included 33 publications, seven of which were RCTs, with the remainder consisting of a combination of non-comparative case

series, comparative cohort studies, and comparative laboratory studies (Karlakki 2013). The most recent systematic review of NPWT for closed surgical wounds included 10 trials and found a reduction in the rate of SSI and seroma in the NPWT group (Hyldig 2016). The review included one trial (Grauhan 2013), which we excluded because it was a quasi-RCT. It also included data that the author obtained from personal correspondence with the investigator of an unpublished trial, to which we had no access. Even though our results were at odds with those from the Hyldig 2016 review, our conclusions remain the same; that is, that the quality of the studies limit any firm conclusions regarding the relative effectiveness of NPWT and standard dressings and further RCTs are required. This conclusion is consistent with evidence-based recommendations for the use of NPWT, which cover a range of applications, including NPWT for acute wounds (Krug 2011), but differs from the latest World Health Organization (WHO) guideline for the prevention of surgical site infection (WHO 2016). The WHO guideline states: "*The panel suggests the use of prophylactic negative pressure wound therapy (pNPWT) in adult patients on primarily closed surgical incisions in high-risk wounds*". However, the recommendation was labelled "conditional" based on a number of issues, including low-quality evidence and the inclusion of non-RCT evidence. Finally, Willy 2017 published international multidisciplinary consensus recommendations suggesting the use of NPWT for a number of patient categories, including those at high risk of SSI. The review contained 100 studies (including RCTs, case series, editorials, cohort studies, technical reports, systematic reviews, and expert opinion), so the conclusions are highly uncertain. In addition, two employees of Acelity, NPWT device manufacturers, were involved in preparing the manuscript, and all of the authors of the review are consultants to an Acelity company (Willy 2017).

AUTHORS' CONCLUSIONS

Implications for practice

Negative pressure wound therapy may reduce the rate of surgical site infection compared with standard wound dressings, but this conclusion is based on low-certainty evidence affected by high risk of bias in the included trials, which were predominantly small. Even greater uncertainty remains about whether negative pressure wound therapy (NPWT) compared with standard dressings reduces most complications associated with surgical incisions, including mortality (very low-certainty evidence). Effect estimates were imprecise, so it is unclear if NPWT reduces or increases the incidence of other important outcomes such as dehiscence or seroma. Effect estimates for the incidence of skin blisters suggest an increase when NPWT is compared with standard dressings, but the evidence is of very low certainty; an increase in dressing cost was also suggested, but is based on very low-certainty evidence. Two studies based on small randomised controlled trials concluded that NPWT may be more cost-effective than standard care when overall resource use is considered. However, there was a high level of uncertainty around the cost estimate, suggesting that larger trials are needed to increase confidence in the results.

Implications for research

Use of NPWT for closed surgical incisions remains a topic of interest, with a very large number of records of ongoing studies identified in our review of clinical trials registries. However, there is a need for further research in this area, as there is a lack of adequately powered, high-quality studies in this field. Future trials could focus initially on wounds that may be difficult to heal, such as sternal wounds or incisions on obese patients. Given the large cost differences between products, further trials comparing different types of NPWT are also justified. Full economic evaluations, including those associated with the NPWT system itself; specialist and other practitioner costs, as measured by time or number of visits; potential cost savings from a change in the number of bed-days in hospital; and costs stemming from differing rates of adverse events and complications (including procedures initiated due to the failure of wounds to heal, such as amputation), need to be included. This will enable users of any future review to gain a clear understanding of the nature of resource use associated with NPWT. To facilitate assessment, future studies that combine different types of conditions (acute, subacute, and chronic) should present the results of each condition group separately.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Chaboyer 2014

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 6 weeks **Sample size estimate:** pilot study **ITT analysis:** yes **number randomised:** 92 **number analysed:** 87 **Funding:** non-industry **Pre-registration:** yes
Participants	**Location:** Queensland, Australia

Chaboyer 2014 *(Continued)*

	Intervention group: n = 35**control group:** n = 35 **Mean age: intervention group** = 30.6 years (IQR 5.5)**control group** = 30.7 years (IQR 5.0) **Inclusion criteria:** booked for elective caesarean section; pre-pregnancy BMI ≥ 30; able to provide consent **Exclusion criteria:** women whose condition changed to require urgent caesarean section; previous participation in the trial; existing infection
Interventions	**Aim/s:** to assess the feasibility of a definitive RCT to test the effectiveness and safety of prophylactic NPWT in obese women after caesarean section **Group 1 (NPWT) intervention:** PICO dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days or longer if drainage continued, unless soiled or dislodged. **Group 2 (control) intervention:** Comfeel dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days or longer if drainage continued, unless soiled or dislodged. **Study date/s:** July 2012 to April 2014
Outcomes	• surgical site infection • type of SSI • hospital readmission • dehiscence; blisters • haematoma **Validity of measure/s:** CDC definitions and criteria for superficial, deep, and organ/space SSI were used for the primary outcome and SF-12 for quality of life. **Time points:** 1, 2, 3, and 4 weeks postsurgery
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote "computer generated 1:1 ratio with blocks of randomly varying sizes"
Allocation concealment (selection bias)	Low risk	A centralised web-based randomised service was accessed.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote "a separate person ... assessed the outcome and was blinded to the allocation"
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 women in the intervention group and 3 in the control group were lost to follow-up, but an ITT analysis was used.

Chaboyer 2014 *(Continued)*

Selective reporting (reporting bias)	Low risk	Planned outcomes reported. Protocol registered on ANZCTR.
Other bias	Low risk	No other biases detected.

Crist 2014

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** ethics approved and consent obtained **Follow-up period:** 12 months **Sample size calculation:** not stated **ITT analysis:** available-case analysis **Funding:** non-industry **Pre-registration:** yes
Participants	**Location:** USA **Intervention group:** n = 55**control group:** n = 60 **Mean age: intervention group** = 47.2 years (SD 19.6)**control group** = 48.3 years (SD 20.1). Data extracted from results section of ClinicalTrials.gov (NCT00635479). **Inclusion criteria:** patients that had undergone an open surgical exposure for hip, pelvis, or acetabular fracture **Exclusion criteria:** none stated
Interventions	**Aim/s:** to determine the effectiveness of using NPWT over primarily closed surgical incisions used for open reduction and internal fixation of hip, pelvis, and acetabular fracture surgery **Group 1 (NPWT) intervention:** quote "negative pressure dressing applied over the primarily closed incision sterilely in the operating room. NPWT was left on for 2 days or longer if drainage continued" **Group 2 (control) intervention:** quote "standard gauze dressing"; description not provided **Study date/s:** not provided
Outcomes	• infection • LOS • total serious adverse events **Validity of measure/s:** not provided **Time points:** followed for 12 months
Notes	Conference abstract. Additional information provided by the investigator and from a search of ClinicalTrials.gov (NCT00635479).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Evidence:** quote "computer randomization" **Comment:** correspondence with author

Crist 2014 *(Continued)*

Allocation concealment (selection bias)	Low risk	**Evidence:** quote "opaquesealed envelope opened in the OR" **Comment:** correspondence with author
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Evidence:** quote "yes" **Comment:** correspondence with author
Incomplete outcome data (attrition bias) All outcomes	High risk	**Evidence:** quote "55 patients randomised to the NPWT group and 60 patients randomised to the standard dressing group. The NPWT group included 49 patients and the gauze group included 42 patients that completed the 12 month follow-up" **Comment:** 10.9% participants in NPWT group and 30.0% of those in control group were lost to follow-up.
Selective reporting (reporting bias)	Low risk	**Comment:** protocol registered on ClinicalTrials.gov with identifier (NCT00635479). Expected outcomes were reported in the abstract, but other outcomes specified in the protocol were not reported (such as total serious adverse events). These may be included when the full trial is published.
Other bias	Unclear risk	**Comment:** no other biases detected

Crist 2017

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** ethics approved and consent obtained **Follow-up period:** not stated **Sample size calculation:** not stated **ITT analysis: number randomised:** 71 **number analysed:** 66 **Funding:** no external funding **Pre-registration:** not stated
Participants	**Location:** USA **Intervention group:** n = 33**control group:** n = 33 **Mean age (range): intervention group** = 44 (19 to 87)**control group** = 43 (18 to 92) **Inclusion criteria:** patients at least 18 years of age with an acetabular fracture that required ORIF **Exclusion criteria:** less than 18 years old; pregnant; unable to provide informed consent; or if their injury could be treated non-operatively or percutaneously
Interventions	**Aim/s:** to determine if iNPWT decreased the risk of deep infection when used over primarily closed surgical incisions for acetabular fracture ORIF **Group 1 (NPWT) intervention:** iNPWT (VAC; KCI, San Antonio, TX) over their surgically closed incision

Crist 2017 *(Continued)*

	Group 2 (control) intervention: a standard postoperative (dry gauze) dressing **Study date/s:** March 2008 to September 2012
Outcomes	• infection **Validity of measure/s:** the clinical diagnosis of infection is determined from the drainage at the operative site in addition to 1 or more of the classic signs and symptoms of inflammation (redness, heat, swelling, pain). Deep infections are those that require operative debridement. Bacteriological cultures obtained at the time of operative debridement. **Time points:** 10 to 21 days, 6 weeks, 12 weeks, and every 6 to 8 weeks thereafter until bony union occurred
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	Approximately 7% of participants were lost to follow-up; reasons for losses were not reported. No more information provided.
Selective reporting (reporting bias)	Low risk	Expected outcomes reported.
Other bias	Low risk	None detected.

DiMuzio 2017

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** not provided **Follow-up period:** 30 days **Sample size calculation:** not stated **ITT analysis: number randomised:** 120 **number analysed:** 120

DiMuzio 2017 *(Continued)*

	Funding: not stated **Pre-registration:** not stated
Participants	**Location:** Philadelphia, USA **Intervention group (high risk):** n = 59**control group (high risk):** n = 60 **(3 arms: low risk:** n = 21**)** **Mean age:** not provided **Inclusion criteria:** femoral incisions closed primarily following elective vascular surgery **Exclusion criteria:** none stated
Interventions	**Aim/s:** to prospectively evaluate negative pressure therapy as a means to decrease wound complications and associated healthcare costs **Group 1 (NPWT) intervention:** NPWT **Group 2 (control) intervention:** standard gauze dressing **Study date/s:** not provided
Outcomes	• infection • LOS • reoperation • readmission **Validity of measure/s:** not provided **Time points:** over 30 days
Notes	Conference abstract

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	140 (3 arms) were enrolled and analysed.
Selective reporting (reporting bias)	Low risk	Planned outcomes reported.
Other bias	Unclear risk	No other biases detected.

Engelhardt 2016

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** ethics approved and consent obtained **Follow-up period:** primary endpoint of the study was the occurrence of SSIs **Sample size calculation:** not stated **ITT analysis:** no **number randomised:** 141 **number analysed:** 132 **Funding:** not stated **Pre-registration:** not stated
Participants	**Location:** Germany **Intervention group (high risk):** n = 64**control group (high risk):** n = 68 **Mean age (range): intervention group** = 72 (64 to 75)**control group** = 70 (60 to 78) **Inclusion criteria:** all consecutive patients scheduled for vascular surgery with a femoral cutdown; age > 18 years and the need for an open, non-emergency surgical procedure for peripheral arterial disease or aneurysm involving the femoral artery using a longitudinal femoral cutdown in the groin **Exclusion criteria:** dementia (not capable of informed consent) and declining to participate
Interventions	**Aim/s:** to determine whether closed-incision negative pressure therapy is able to reduce SSI rate in the groin after vascular surgery **Group 1 (NPWT) intervention:** NPWT was applied on the closed skin intraoperatively. The system is comprised of a therapy unit containing a pump with a 45-millilitre canister delivering a continuous negative pressure of 125 mmHg and a self adhesive dressing with a foam bolster that manifolds the negative pressure to the incision area. A special polyester interface layer protects the skin from direct contact with the foam bolster, while at the same time allowing delivery of negative pressure and fluid removal. **Group 2 (control) intervention:** absorbent adhesive dressing **Study date/s:** January 2012 and October 2014
Outcomes	• infection **Validity of measure/s:** all wounds were documented with photos and classified according to the Szilagyi classification. Grade I infections only involved the skin (dermal infection); grade II extended to the subcutaneous tissue without reaching the vessels; and grade III finally involved the artery or bypass. **Time points:** 5th postoperative day and 6 weeks after surgery
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random assignment of the participants to the 2 treatment groups was performed according to an external randomisation sequence.
Allocation concealment (selection bias)	Low risk	Sealed randomisation envelopes were provided by an external institution. On eligibility confirmation, the sequential randomisation envelope was opened, and the assignment was allocated.

Engelhardt 2016 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "all wounds were documented by photography and classified according to the Szilagyi classification" **Comment:** unclear whether outcome assessment was blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	ITT not used; 141 participants were randomised, and 132 completed the study; 9 participants (6%) did not complete follow-up due to urgent reoperation or death during follow-up.
Selective reporting (reporting bias)	Low risk	Planned outcomes reported.
Other bias	Low risk	None detected.

Frazee 2018

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** ethics approved and consent obtained **Follow-up period:** primary endpoint of the study was the occurrence of SSIs **Sample size calculation:** not stated **ITT analysis:** yes **number randomised:** 49 **number analysed:** 49 **Funding:** not stated **Pre-registration:** not stated
Participants	**Location:** Texas, USA **Intervention group (high risk):** n = 24 (open-NPWT)**control group (high risk):** n = 25 (closed-NPWT) **Mean age: intervention group** = 54**control group** = 60 **Inclusion criteria:** patients undergoing celiotomy with either class III or class IV surgical wounds **Exclusion criteria:** not stated
Interventions	**Aim/s:** to evaluate speed of wound healing as well as any deleterious effects of closed-wound management **Group 1 (open-NPWT) intervention:** open wounds received negative pressure wound therapy dressings consisting of a KCl black sponge covered by wound V.A.C. film (KCl) and attached to a negative pressure pump. These dressings were changed 3 times per week. **Group 2 (closed-NPWT) intervention:** the PREVENA dressing was placed at the time of closure, and remained in place for 7 days, at which time it was removed and the wound was left open to air. **Study date/s:** not stated
Outcomes	• time to complete wound healing • wound infection

Frazee 2018 *(Continued)*

- seroma
- dehiscence

Validity of measure/s: time to wound healing defined as complete epithelisation of the wound and staples/dressings removed.

Time points: participants were followed to complete wound healing or time of death.

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomised within wound category by computer generated randomizations forms"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	An ITT analysis was used.
Selective reporting (reporting bias)	Low risk	Planned outcomes reported.
Other bias	Low risk	None detected.

Gillespie 2015

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 6 weeks **Sample size estimate:** pilot study **ITT analysis:** yes **number randomised:** 70 **number analysed:** 70 **Funding:** non-industry **Pre-registration:** yes
Participants	**Location:** Queensland, Australia

Gillespie 2015 *(Continued)*

	Intervention group: n = 35**control group:** n = 35 (primary hip arthroplasty) **Mean age: intervention group** = 30.6 years (SD 5.5)**control group** = 30.7 years (SD 5.0) **Inclusion criteria:** booked for elective caesarean section; pre-pregnancy BMI ≥ 30; able to provide consent **Exclusion criteria:** women whose condition changed to require urgent caesarean section; previous participation in the trial; existing infection; unable to speak English
Interventions	**Aim/s:** to determine the feasibility of conducting a larger trial **Primary outcome/s:** surgical site infection **Secondary outcome/s:** type of SSI; wound complications; hospital length of stay; hospital readmission **Group 1 (NPWT) intervention:** PICO dressing applied over the primarily closed incision by the surgeon in the operating room. On day 5 the dressing was changed to OPSITE Post-Op Visible. **Group 2 (control) intervention:** Comfeel dressing reinforced with 2 absorbent dressings, and then with a self adhesive, non-woven tape, which was applied over the primarily closed incision by the surgeon in the operating room. Participants were discharged with their dressing intact. **Study date/s:** March 2013 to May 2014
Outcomes	• SSI • bruising • bleeding • dehiscence • blisters • haematoma • seroma • hospital readmission • Cost of dressings **Validity of measure/s:** CDC definitions and criteria for superficial, deep, and organ/space SSI were used for the primary outcome and SF-12 for quality of life (QoL reported in the Heard 2017 study). **Time points:** 30 days and 6 weeks postsurgery
Notes	Investigator contacted for additional details.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer generated randomised schedule 1:1 ratio in randomly varying blocks was prepared by the statistician on the research team (not involved in recruitment)"
Allocation concealment (selection bias)	Low risk	Quote: "on skin closure, the RNA opened the next sealed, opaque, numbered envelope"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias)	Low risk	Quote: "the independent outcome assessors as well as the data analyst were blinded to group allocation"

Gillespie 2015 *(Continued)*
All outcomes

Incomplete outcome data (attrition bias) All outcomes	Low risk	An ITT analysis was used.
Selective reporting (reporting bias)	Low risk	Planned outcomes reported. Protocol pre-registered on ANZCTR.
Other bias	Low risk	None detected.

Gunatilake 2017

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 42 ± 10 days **Sample size estimate:** not stated **ITT analysis:** yes **number randomised:** 92 **number analysed:** 92 **Funding:** non-industry **Pre-registration:** yes
Participants	**Location:** Texas, USA **Intervention group:** n = 46**control group:** n = 46 **Mean age (SD): intervention group** = 30.4 (5.7)**control group** = 29.7 (5) **Inclusion criteria:** 18 years of age with BMI 35 kg/m^2 at the time of delivery **Exclusion criteria:** women with skin or systemic infections, chorioamnionitis (defined by maternal fever + 1 clinical criteria), critical illness, or high-risk for anaesthesia (ASA class P4, P5, or P6)
Interventions	**Aim/s:** to compare short-term clinical outcomes among obese pregnant women undergoing caesarean delivery who received ciNPT or a standard-of-care dressing **Primary outcome/s:** SSO: unanticipated local inflammation, wound infection, seroma, haematoma, dehiscence, and need for surgical or antibiotic intervention **Secondary outcome/s:** not stated **Group 1 (NPWT) intervention:** a sterile, "peel-and-place" multilayer dressing (wicking fabric, reticulated foam, and adhesive) was placed over participant's closed incision. The dressing's tubing was then attached to a compact, portable negative pressure therapy unit that delivered 125 mmHg of continuous pressure to the dressing and removed exudates into a disposable canister. Duration of ciNPT was 5 to 7 days, immediately following surgery. **Group 2 (control) intervention:** Steri-Strips (3M Health Care, ½ inch, St Paul, MN), sterile gauze, and Tegaderm (3M Health Care, transparent film dressings (non-penetrable barrier)) were applied to the closed surgical incision for at least 1 day and no longer than 2 days. **Study date/s:** between 2012 and 2014
Outcomes	• postoperative SSOs: included unanticipated local inflammatory response, prolonged drainage, fluid collection, dehiscence, and surgical site intervention • surgical interventions: included antimicrobials for SSI, surgical drainage of the incision, surgical incision packing, adjunctive negative-pressure therapy, debridement, or reoperation

Gunatilake 2017 *(Continued)*

	Validity of measure/s: wound scoring system; surgical site assessments included the supplementary outcomes of incisional pain scores at rest and with pressure on the closed incision, as measured by the Wong–Baker Faces Scale **Time points:** all participants were followed up postoperatively for 42 ± 10 days via periodic incisional assessments (postoperative days 1, 2, 6, 14, and 42).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Study personnel obtained the next sequentially numbered, opaque randomisation envelope, which contained the randomly assigned treatment group for the participant.
Allocation concealment (selection bias)	Unclear risk	Study personnel obtained the next sequentially numbered, opaque randomisation envelope, which contained the randomly assigned treatment group for the participant.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Although the postoperative examiner was privy to the treatment group, a standardised wound scoring system was utilised to minimise bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	An ITT analysis was used.
Selective reporting (reporting bias)	Unclear risk	Planned outcomes reported. Protocol pre-registered on ClinicalTrials.gov (identifier NCT01450631).
Other bias	Low risk	None detected.

Heard 2017

Methods	**Study design:** randomised controlled trial. Data drawn from the Chaboyer 2014 RCT. **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 6 weeks **Sample size estimate:** pilot study **ITT analysis:** yes **number randomised:** 92 **number analysed:** 87 **Funding:** non-industry **Pre-registration:** yes

Heard 2017 *(Continued)*

Participants	**Location:** Queensland, Australia **Intervention group:** n = 46**control group:** n = 46 (obese women (> 30 BMI) undergoing elective CS) **Mean age: intervention group** = 30.6 years (SD 5.5)**control group** = 30.7 years SD 5.0) **Inclusion criteria:** booked for elective CS; pre-pregnancy BMI > 30; able to provide consent **Exclusion criteria:** women whose condition changed to require urgent CS; previous participation in the trial; existing infection
Interventions	**Aim/s:** "to evaluate whether NPWT is cost-effective compared with standard care in obese women undergoing caesarean section" **Group 1 (NPWT) intervention:** PICO dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days, or longer if drainage continued, unless soiled or dislodged. **Group 2 (control) intervention:** Comfeel dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days, or longer if drainage continued, unless soiled or dislodged. **Study date/s:** July 2012 to April 2014
Outcomes	• cost-effectiveness **Validity of measure/s:** SF-12 for quality of life **Time points:** 1, 2, 3, and 4 weeks postsurgery
Notes	Quality rating according to the CHEERS checklist was 83.3%.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer generated 1:1 ratio with blocks of randomly varying sizes"
Allocation concealment (selection bias)	Low risk	A centralised web-based randomised service was accessed.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "a separate person ... assessed the outcome and was blinded to the allocation"
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 women in the intervention group and 3 in the control group were lost to follow-up, but an ITT analysis was used.
Selective reporting (reporting bias)	Low risk	Planned outcomes reported. Protocol registered on ANZCTR.
Other bias	Low risk	No other biases detected.

Howell 2011

Methods	**Study design:** randomised controlled trial **Ethics and informed consent:** not reported **Sample size calculation:** yes **Follow-up period:** 12 months **ITT analysis:** all participants completed the study. **Funding:** the study was supported by KCI, the manufacturer of the negative pressure device.
Participants	**Location:** NYU Hospital for Joint Disorders, New York, NY, USA **Intervention group:** n = 24**control group:** n = 36 **Mean age:** not reported **Inclusion criteria:** patients undergoing unilateral or bilateral primary total knee arthroplasty who were obese (BMI > 30), who met criteria of increased risk for postoperative wound drainage and who were prescribed enoxaparin sodium for deep vein thrombosis prophylaxis **Exclusion criteria:** patient refusal to participate in the study, revision total knee replacement, prior knee surgery (except arthroscopy), and patients with documented diabetes mellitus
Interventions	**Aim/s:** to compare the number of days to dry wound in a negative pressure dressings group compared with a static pressure dressings group **Intervention/s in both groups:** "all patients received three doses of peri-operative intravenous antibiotics and were maintained on subcutaneous DVT prophylaxis for 30 days after surgery" **Group 1 (NPWT) intervention:** "subsequent to the closure of the surgical incision, a negative pressure dressing (VAC Therapy, Kinetic Concepts Inc., San Antonio, Texas) was applied under sterile conditions. A medical grade open cell polyurethane ether foam (pore size of 400-600 micrometers) was cut into the shape of a rectangle approximately 5 cm in width and a length sufficient to cover the entire linear wound. The knee was held in 151° of flexion, and the foam was secured over the incision by the application of a specialized adhesive drape, provided in the NPWT system. An evacuation tube with side ports was embedded within the reticulated foam, allowing negative pressure to be applied equally over the entire wound bed. The foam-evacuation tube complex attached to a programmable vacuum pump applied a −125 mmHg continuous vacuum pressure to the wound. The NPWT dressing remained in place for a 48-hour period, after which time clean, dry gauze dressings were applied and changed on daily basis until the wound was dry" **Group 2 (SPD) intervention:** "patients in the control arm had their surgical wound covered in the operating room with a sterile, dry gauze dressing that was held in place with a perforated, stretchable cloth tape. This initial dressing remained in place for 48 hours after which time clean, dry gauze dressings were applied and changed on a daily basis until the wound was dry" **Study date/s:** not stated
Outcomes	• days to dry wound • deep wound infection • blister formation **Time points:** participants followed up for 12 months postsurgery.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	**Comment:** not described

Howell 2011 *(Continued)*

Allocation concealment (selection bias)	Low risk	Quote: "randomised with blinded envelopes to either the treatment with negative pressure wound therapy group or a control group using sterile gauze"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes **Comment:** difference in appearance of dressings made blinding impossible.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Evidence:** not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Evidence:** 51 participants were randomised, and 51 completed the study.
Selective reporting (reporting bias)	Low risk	**Comment:** the prespecified clinical outcomes were presented in Table 1 in the trial report, and a post hoc analysis of blister occurrence was shown in Table 2. Infection rates were reported in the results section of the trial report. We could not find a published protocol.
Other bias	High risk	No baseline data were presented. In addition, groups contained unequal numbers, which could indicate undisclosed losses in 1 group.

Hussamy 2017

Methods	**Study design:** randomised controlled trial **Ethics and informed consent:** not reported **Sample size calculation:** yes **Follow-up period:** not stated **ITT analysis:** yes **Funding:** not stated
Participants	**Location:** Texas, USA **Intervention group:** n = 222**control group:** n = 219 **Mean age:** not reported **Inclusion criteria:** women with class III obesity (BMI > 40 kg/m^2) undergoing caesarean delivery **Exclusion criteria:** women on anticoagulation, with HIV infection, sensitive skin disorders, or silver or acrylic allergies
Interventions	**Aim/s:** to compare the efficacy of closed incision negative pressure therapy (ciNPT) with a standard surgical dressing in the prevention of postoperative wound morbidity in women with class III obesity undergoing caesarean delivery **Group 1 (NPWT) intervention:** a ciNPT dressing at time of caesarean **Group 2 (control) intervention:** a standard surgical dressing **Study date/s:** January 2015 to July 2016 (18 months)

Hussamy 2017 *(Continued)*

Outcomes	• wound morbidity including wound disruption requiring the use of antimicrobials, prolonged postoperative hospitalisation, hospital readmission, or reoperation within 30 days of delivery **Validity of measure/s:** not stated **Time points:** not stated
Notes	Only the abstract was available.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	441 participants were enrolled and analysed.
Selective reporting (reporting bias)	Low risk	Expected outcomes were reported in the abstract.
Other bias	Unclear risk	Not stated

Karlakki 2016

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 6 weeks **Sample size estimate:** pilot study **ITT analysis:** yes **number randomised:** 220 **number analysed:** 209 **Funding:** study funded through a grant from Smith & Nephew UK to cover the cost of NPWT dressings and data collection costs. 2 investigators declared they had funding and consultancy fees from Smith & Nephew. **Pre-registration:** no

Karlakki 2016 *(Continued)*

Participants	**Location:** Oswestry, UK **Intervention group:** n = 110**control group:** n = 110 **Mean age (SD): intervention group** = 69 (9.0)**control group** = 69.2 (9.0) **Inclusion criteria:** patients undergoing total hip or knee arthroplasties (for any indication) with any of 3 consultant surgeons **Exclusion criteria:** patients who had known allergies to dressing, were undergoing revision joint surgery, were unwilling to attend additional clinics, and those on warfarin were excluded.
Interventions	**Aim/s:** to evaluate the effectiveness of incisional negative pressure wound therapy dressing (iNPWTd) **Group 1 (NPWT) intervention:** PICO dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days, or longer if drainage continued, unless soiled or dislodged. **Group 2 (control) intervention:** Comfeel dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days, or longer if drainage continued, unless soiled or dislodged. **Study date/s:** July 2012 to April 2014
Outcomes	• SSI • blisters • haematoma • hospital readmission **Validity of measure/s:** not described **Time points:** 1, 2, and 6 weeks postsurgery
Notes	Investigator contacted for additional details.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the randomisation was performed using sealed opaque envelopes with a block size of 20 shuffled envelopes" **Comment:** no sequence generation was required.
Allocation concealment (selection bias)	Low risk	Quote: "the randomisation was performed using sealed opaque envelopes with a block size of 20 shuffled envelopes" **Comment:** allocation was unknown until envelope opened.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were aware of group allocation.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	7.3% in intervention group and 2.7% in control group PP analysis

Karlakki 2016 *(Continued)*

		Comment: more participants were excluded from the analysis in the intervention group (8 intervention vs 3 control).
Selective reporting (reporting bias)	Low risk	Expected outcomes reported.
Other bias	High risk	Intervention participants were seen in a wound clinic at 1 week, and control participants were not.

Kuncewitch 2017

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** not reported **Follow-up period:** not reported **Sample size estimate:** not reported **ITT analysis:** yes **number randomised:** 73 **number analysed:** 73 **Funding:** not reported **Pre-registration:** not reported
Participants	**Location:** not reported **Intervention group:** n = 36**control group:** n = 37 **Mean age (SD):** not reported **Inclusion criteria:** high-risk surgical oncology patients undergoing laparotomy **Exclusion criteria:** not stated
Interventions	**Aim/s:** to investigate the effects of NPWT on short- and long-term wound outcomes in people undergoing pancreatectomy **Group 1 (NPWT) intervention:** NPWT **Group 2 (control) intervention:** standard surgical dressing **Study date/s:** 2012 to 2016
Outcomes	• postoperative wound complications in the first 30 days • incisional hernia rates • rates of pancreatic fistula • delayed gastric emptying **Validity of measure/s:** not described **Time points:** not stated
Notes	Only the abstract was available.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated

Kuncewitch 2017 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	73 participants were enrolled and analysed.
Selective reporting (reporting bias)	Low risk	Expected outcomes were reported in the abstract.
Other bias	Unclear risk	Abstract only

Lee 2017a

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 6 weeks **Sample size estimate:** not reported **ITT analysis:** no **number randomised:** 60 **number analysed:** 44 **Funding:** KCI USA Incorporated, an Acelity company **Pre-registration:** yes
Participants	**Location:** Canada **Intervention group:** n = 33**control group:** n = 27 **Mean age (± SD): intervention group** = 67.1 (± 7.2)**control group** = 68.3 (± 9.7) **Inclusion criteria:** receiving an isolated elective or semi-elective CABG and above 18 years of age living within 1 hour of the institution **Exclusion criteria:** emergent surgery, previous CABG or lower leg surgical intervention, severe peripheral vascular disease, dialysis-dependent renal failure, and chronic steroid administration
Interventions	**Aim/s:** to establish the safety and feasibility of using NPWT on the GSV harvest site postcardiac surgery and to examine the effects on infection, complications, and overall patient function **Group 1 (NPWT) intervention:** NPWT device was placed at the time of GSV harvest in the operating room and then maintained in situ until the day prior to hospital discharge or to a maximum of 7 days. The device was removed if poorly tolerated by the participant or for any safety concerns. **Group 2 (control) intervention:** conventional dry gauze dressings **Study date/s:** not stated

Lee 2017a *(Continued)*

Outcomes	• rates of device complication and malfunction • rates of SSI, lower leg complications, discharge date, and quality of life at discharge and 6 weeks **Validity of measure/s:** complications were classified as major if they required a medical or surgical intervention. All complications and device malfunctions were recorded. The total length of therapy with the NPWT device was recorded, and also if therapy was prematurely interrupted for any reason. SSIs was determined through assessment of the ASEPSIS score. The incidence of leg complications was also examined including pain, heaviness, weakness, stiffness, itching, paraesthesia, numbness, burning, discolouration, rash, and oedema. These complications were graded as 'not present', 'mild', 'moderate', and 'severe'. Only the moderate and severe complaints were included for incidence analysis. Discharge dates were also recorded for all participants. Self reported assessments of mobility, overall pain or discomfort, feelings of anxiety or depression, ability for self care, and ability to perform usual activities were performed. These measures were graded as no issues, some issues, and severe issues or inability. Quality of life was also measured using the EQ-5D-3L Measure of Health Status. **Time points:** initial and 6 weeks
Notes	33 vs 27 participants randomised; high loss to follow-up recorded

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Consented patients were randomised by use of sealed ballot envelopes in a 1-to-1 fashion.
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	A research assistant blinded to the grouping assessed the incision and participant prior to discharge and at 6 weeks postoperatively. A second, unblinded research assistant recorded and managed any device-related complications. Participants were discharged based on standardised institutional discharge criteria.
Incomplete outcome data (attrition bias) All outcomes	High risk	12 participants were lost to follow-up at 6 weeks, 4 in the NPWT group and 8 in the control group. These participants were not included in the data analysis.
Selective reporting (reporting bias)	Low risk	Planned outcomes reported. Protocol registered on ClinicalTtrials.gov (NCT01698372).
Other bias	High risk	High loss to follow-up without reasons for loss being provided

Lee 2017b

Methods	**Study design:** randomised controlled trial

Lee 2017b *(Continued)*

	Study grouping: parallel **Ethics and informed consent:** yes **Follow-up period:** 90 days **Sample size estimate:** yes **ITT analysis:** no **number randomised:** 102 **number analysed:** 102 **Funding:** not company funded **Pre-registration:** yes
Participants	**Location:** Canada **Intervention group:** n = 53**control group:** n = 49 **Mean age: intervention group** = 69 ± 10**control group** = 68 ± 10 **Inclusion criteria:** patients with 1 of the following 3 risk factors for SSIs were enrolled in the trial: obesity defined as a BMI of > 30 kg/m^2, previous femoral artery exposure, or presence of minor or major ischaemic tissue loss. **Exclusion criteria:** patients with pre-existing groin infection, a known allergy to dressing material, or those who could not be followed postoperatively were excluded from the study.
Interventions	**Aim/s:** to perform an RCT to study the role of NPWT on SSI in primarily closed groin incisions after lower extremity revascularisation in vascular surgery patients **Group 1 (NPWT) intervention:** NPWT remained on until either hospital discharge or postoperative day 8, whichever occurred earlier. **Group 2 (control) intervention:** standard gauze dressing (the dressing removed on postoperative day 2, and then had daily dressing changes with inspection of the wound) **Study date/s:** August 2014 to December 2015
Outcomes	• the incidence of SSI within 30 days of revascularisation • duration of hospital stay • SSI within 90 days • reoperation and readmission rate owing to SSI within 90 days • mortality within 90 days **Validity of measure/s:** SSI was diagnosed using the CDC guideline as a superficial or deep infection. The Szilagyi classification of vascular wound infection was also used to classify the infection. **Time points:** once discharged, both groups were followed up in the clinic at 30 and 90 postoperative days.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Eligible patients were randomised to NPWT or a standard sterile gauze dressing using an internet-based software, sealedenvelope.com (London, UK), using block randomisation.
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias)	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes

Lee 2017b *(Continued)*

All outcomes		**Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Wounds were inspected at each clinic visit by a wound specialist nurse who was blinded to the treatment groups. If she was uncertain, the staff physician determined the presence or absence of an SSI. An SSI could also be diagnosed by the patient care team if there were clinical signs and symptoms of infection.
Incomplete outcome data (attrition bias) All outcomes	Low risk	102 participants were enrolled and analysed.
Selective reporting (reporting bias)	Low risk	Planned outcomes reported. Protocol registered on ClinicalTrials.gov (NCT02084017).
Other bias	Low risk	No other biases detected.

Leon 2016

Methods	**Study design:** prospective, randomised, multicentre study **Study grouping:** parallel **Ethics and informed consent:** not reported **Follow-up period:** not reported **Sample size estimate:** not reported **ITT analysis:** yes **number randomised:** 81 **number analysed:** 81 **Funding:** not reported **Pre-registration:** not reported
Participants	**Location:** Spain **Intervention group:** n = 47**control group:** n = 34 **Mean age (SD):** not reported **Inclusion criteria:** patients undergoing open and programmed colorectal surgery **Exclusion criteria:** not stated
Interventions	**Aim/s:** to evaluate the benefits of negative pressure therapy to reduce surgical site infection rate in open colorectal surgery **Group 1 (NPWT) intervention:** NPWT **Group 2 (control) intervention:** usual dressing group **Study date/s:** not reported
Outcomes	• SSI rate **Validity of measure/s:** not described **Time points:** a daily evaluation through hospitalisation and a 15- and 30-day evaluation
Notes	Only the abstract was available.

Risk of bias

Leon 2016 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All enrolled participants were accounted for in the analyses.
Selective reporting (reporting bias)	Unclear risk	Not stated
Other bias	Unclear risk	Abstract only

Lozano-Balderas 2017

Methods	**Study design:** randomised controlled trial **Ethics and informed consent:** ethics approved **Sample size calculation:** no **ITT analysis:** yes **number randomised:** 81 **number analysed:** 81 **Follow-up period:** healed (when in hospital) or in a 30-day period after surgery (if discharged) **Funding:** non-industry **Pre-registration:** yes
Participants	**Location:** Mexico **Intervention group:** n = 25**control group:** n = 27 **(3 arms: delayed primary closure group:** n = 29**)** **Median age (IQR): intervention group** = 32 (22 to 46);**control group** = 30 (20 to 43) **Inclusion criteria:** minimum age of 18; a laparotomised wound with class III or IV (contaminated/dirty-infected) surgical wounds **Exclusion criteria:** not specified
Interventions	**Aim/s:** to compare infection rates between primary, delayed primary, and vacuum-assisted closures in contaminated/dirty-infected surgical wounds **Group 1 (NPWT) intervention:** the VAC was used with routine changes of dressings every 48 hours until healthy granulation tissue was found and a surgeon decided to close it.

Lozano-Balderas 2017 *(Continued)*

	Group 2 (control) intervention: subcutaneous tissue was approximated with polyglycolic acid, and polypropylene was used for the skin. **Study date/s:** January to July 2014
Outcomes	• SSI **Validity of measure/s:** according to the CDC Surgical Wound Classification **Time points:** daily when in hospital or in a 30-day period after surgery
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were allocated to each group with the software Research Randomizer® (Urbaniak, G. C., & Plous, S., Version 4.0)"
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were aware of group allocation.
Incomplete outcome data (attrition bias) All outcomes	Low risk	81 participants were enrolled and analysed.
Selective reporting (reporting bias)	Low risk	Expected outcomes reported. Protocol retrospectively registered on ClinicalTrials.gov (NCT02649543).
Other bias	Low risk	No other biases detected.

Manoharan 2016

Methods	**Study design:** randomised controlled trial **Study grouping:** bilateral knees were randomised to intervention or control knees **Ethics and informed consent:** yes **Sample size estimate:** yes, but sample did not reach target, stopped due to financial constraints **Follow-up period:** 10 days **ITT analysis:** yes **number randomised:** 21 **number analysed:** 21 **Funding:** KCI, Acelity Inc provided the negative pressure wound therapy dressings for the study.

Manoharan 2016 *(Continued)*

	Pre-registration: retrospectively registered as ANZCTR 12615001350516
Participants	**Location:** Queensland, Australia **Intervention group:** n = 21 knees**control group:** n = 21 knees **Mean age (range):** 66 (45 to 80) **Inclusion criteria:** patients undergoing a bilateral knee arthroplasty **Exclusion criteria:** aged < 18 years or pregnant
Interventions	**Aim/s:** to assess the effect of NPWT on outcomes after primary arthroplasty **Group 1 (NPWT) intervention:** the intervention group received PREVENA Incision Management System, Acelity, KCI, which was placed over the closed surgical incision under sterile conditions at the end of the procedure. The NPWT device provided a continuous negative pressure of 125 mmHg for a duration of 8 days. **Group 2 (control) intervention:** the conventional dry dressing was placed over the closed surgical incision under sterile conditions at the end of the procedure. Neither the type of control dressing nor when the dressing was removed was reported. **Study date/s:** February to December 2014
Outcomes	• SSI • blisters • cost • QoL **Validity of measure/s:** no **Time points:** 10 to 12 days postsurgery
Notes	Investigator contacted for additional details.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Simple randomisation was performed by the research assistants via online computer software that indicated the side to which the intervention, NPWT, would be applied.
Allocation concealment (selection bias)	High risk	The surgeons were notified on the day of surgery, before the commencement of the procedure. It was also unclear if consecutive patients for each of the 3 surgeons were recruited.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	High risk	The final incision assessment was performed by the surgeon and clinic nurse and witnessed by 1 of the research assistants. There were no independent observers attached to this assessment.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	It was unclear if all participants were accounted for in the results as the numbers analysed for each outcome are not stated.

Manoharan 2016 *(Continued)*

Selective reporting (reporting bias)	Low risk	Expected outcomes reported. Protocol retrospectively registered as ANZCTR 12615001350516.
Other bias	Low risk	No other biases detected.

Masden 2012

Methods	**Study design:** randomised controlled trial **Ethics and informed consent:** the study was approved by the Georgetown University Institutional Review Board. Consent was not specifically stated, but those patients not capable of undergoing informed consent were excluded. **Sample size calculation:** yes **Follow-up period:** mean 113 days **ITT analysis:** available-case analysis **Funding:** 2 of the investigators are consultants for KCI, and the study was funded by the manufacturer of the intervention product.
Participants	**Location:** Columbus, Ohio, USA **Intervention group:** n = 50**control group:** n = 43 **Mean age: intervention group** = 61.3 years (range 40 to 101)**control group** = 61.3 years (range 38 to 86) **Inclusion criteria:** patients scheduled to undergo radial forearm free flap **Exclusion criteria: "**patients not capable of undergoing informed consent and those patients with tape allergies or who otherwise could not tolerate NPWT ... patients with lower extremity amputations distal to the forefoot were excluded"
Interventions	**Aim/s:** to evaluate the effect of NPWT on closed surgical incisions. Prospective randomised controlled clinical trial comparing NPWT to standard dry dressings on surgical incisions **Primary:** "to evaluate the effectiveness of NPWT in patients with multiple co morbidities" **Secondary:** "to evaluate factors that contribute to wound complication" **Intervention/s in both groups:** "the graft was covered with a single layer of paraffin gauze dressing (Jelonet, Smith & Nephew, UK); then, 3 sheets of polyurethane (high-density foam, Nuris Luisa, Santiago, Chile) with a fenestrated silicone drainage tube between the layers was placed over the gauze and covered with a transparent adhesive dressing (Opsite, Smith & Nephew, UK) providing the vacuum seal. We used a double layer under the tube to prevent pressure ulcers at the bed of the suction tube" **Group 1 (NPWT) intervention:** "NPWT group ... underwent placement of a V.A.C. system (KCI, San Antonio, Texas) along the line of closure set at −125mmHg continuous pressure at the time of closure" **Group 2 (control) intervention:** "the control group ... received a standard dry sterile dressing consisting of a non adhesive silicone layer (Mepitel, Mölnlycke Health Care AB, Göteborg, Sweden) and a bacteriostatic single silver layer (Acticoat, Smith & Nephew, Hull, UK)" **Study date/s:** October 2008 to August 2010
Outcomes	• wound infection • dehiscence • reoperation • LOS **Validity of measure/s:** not stated

Masden 2012 *(Continued)*

	Time points: "all incisions assessed on the third postoperative day ... and reassessed at the first outpatient postoperative visit, as well as any subsequent visit (the last recorded infection was at 66 days post surgery)". However, the abstract states that "average follow-up was 113 days".
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Evidence:** quote (from correspondence with the author): "used a randomization generator through Excel in groups of 8 (4 controls, 4 experimental)" **Comment:** adequate method
Allocation concealment (selection bias)	Low risk	**Evidence:** quote (from correspondence with the author): "when the patient was recruited ... they contacted one of the investigators and the patient was assigned to whichever group was next on the list" **Comment:** adequate method
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Evidence:** quote: "the evaluations were performed by a member of the research team not involved in the enrolment or the operative treatment and, thus, were blinded as to randomization group" **Comment:** adequate method
Incomplete outcome data (attrition bias) All outcomes	Low risk	**Evidence:** quote: "twelve subjects were lost to follow up in the immediate postoperative period and were excluded from the final analysis" **Comment:** equal number of losses in both groups
Selective reporting (reporting bias)	Low risk	**Comment:** protocol unavailable, but expected outcomes reported
Other bias	Unclear risk	**Comment:** the standard dressing contained a silver layer, which may have influenced the outcome.

Nherera 2017

Methods	**Study design:** randomised controlled trial (economic evaluation based on the Karlakki 2016 RCT) **Study grouping:** parallel **Ethics and informed consent:** yes **Follow-up period:** 6 weeks **Sample size estimate:** pilot study **ITT analysis:** yes **number randomised:** 220 **number analysed:** 209

Nherera 2017 *(Continued)*

	Funding: study funded through a grant from Smith & Nephew, UK, to cover the cost of NPWT dressings and data collection costs. 2 investigators declared they had funding and consultancy fees from Smith & Nephew. **Pre-registration:** no
Participants	**Location:** Oswestry, UK **Intervention group:** n = 110**control group:** n = 110 **Mean age (SD): intervention group** = 69 (9.0)**control group** = 69.2 (9.0) **Inclusion criteria:** patients undergoing THAs or TKAs (for any indication) with 3 consultant surgeons (SLK, NMG, and RDB – authors of this study) **Exclusion criteria:** patients who had known allergies to dressing, were undergoing revision joint surgery, were unwilling to attend additional clinics, and those on warfarin were excluded.
Interventions	**Aim/s:** to evaluate the cost-effectiveness of incisional NPWT dressing **Group 1 (NPWT) intervention:** PICO dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days, or longer if drainage continued, unless soiled or dislodged. **Group 2 (control) intervention:** Comfeel dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days, or longer if drainage continued, unless soiled or dislodged. **Study date/s:** July 2012 to April 2014
Outcomes	• cost-effectiveness
Notes	The first 2 authors are employed by Smith & Nephew, UK (manufacturers of the intervention product). Quality rating using the CHEERS checklist was 85.4%.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "the randomisation was performed using sealed opaque envelopes with a block size of 20 shuffled envelopes" **Comment:** unclear how the random sequence was generated
Allocation concealment (selection bias)	High risk	Quote: "the randomisation was performed using sealed opaque envelopes with a block size of 20 shuffled envelopes" **Comment:** surgeons knew at the start of the surgery to which group participants had been randomised.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were aware of group allocation.
Incomplete outcome data (attrition bias)	Unclear risk	7.3% in intervention group and 2.7% in control group based on a PP analysis

Nherera 2017 *(Continued)*

All outcomes		**Comment**: more intervention participants were excluded from the analysis (8 intervention vs 3 control).
Selective reporting (reporting bias)	Low risk	Stated outcomes were reported.
Other bias	Low risk	No other biases detected.

Nordmeyer 2016

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Sample size estimate:** no **Follow-up period:** unknown **ITT analysis:** yes **number randomised:** 20 **number analysed:** unclear **Funding:** unclear. MHB gave scientific presentations for KCI. **Pre-registration:** no
Participants	**Location:** Nuremberg, Germany **Intervention group:** n = 10**control group:** n = 10 **Mean age: intervention group** = 52.3 (16.3)**control group** = 57.8 (15.2) **Inclusion criteria:** patients with spinal fractures who were scheduled for internal fixation **Exclusion criteria:** not reported
Interventions	**Aim/s:** to evaluate the different aspects of wound healing in spinal fractures treated with internal fixation **Group 1 (NPWT) intervention:** the iNPWT group was treated with a PICO system (Smith & Nephew, UK). The PICO system was left on the wound for 5 days including the day of surgery. In addition to daily clinical examination, all wounds/seroma were analysed by ultrasonography on day 5 and day 10 after surgery. **Group 2 (control) intervention:** standard department wound dressing consisting of dry wound coverage (compresses attached to the skin) was used. **Study date/s:** not reported
Outcomes	• seroma **Validity of measure/s:** ultrasound was used as a standardised imaging modality to detect seromas in the wound area. **Time points:** day 5 and day 10 after surgery
Notes	Investigator contacted for additional details.

Risk of bias

Bias	Authors' judgement	Support for judgement

Nordmeyer 2016 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Numbers analysed were not reported.
Selective reporting (reporting bias)	High risk	Only seroma reported, not wound infection.
Other bias	Low risk	None identified.

O'Leary 2017

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Sample size estimate:** yes, but it was based on a reduction in SSI from 35% to 10% **ITT analysis:** yes **number randomised:** 50 **number analysed:** 49 **Follow-up period:** 30 days **Funding:** support was received from Smith & Nephew. The authors were responsible for trial design, data analysis, and manuscript writing. The decision to publish trial results was made between study authors and study sponsors. **Pre-registration:** ClinicalTrials.gov registration NCT02780453 (registered after study completed – May 2016)
Participants	**Location:** Limerick, Ireland **Intervention group:** n = 25**control group:** n = 25 **Mean age: intervention group** = 58 (range 31 to 73)**control group** = 63 (range 33 to 76) **Inclusion criteria:** patients undergoing elective or emergency open abdominal surgery with a clean, clean-contaminated, or contaminated wound **Exclusion criteria:** dirty wound; BMI ≥ 40; ASA grade > 3
Interventions	**Aim/s:** to assess the effect of NPWT on SSI

O'Leary 2017 *(Continued)*

	Group 1 (NPWT) intervention: PICO dressing (Smith & Nephew) was applied to the wound by the operating surgeon, and the edges of the dressing were reinforced with self adherent tape. **Group 2 (control) intervention:** transparent waterproof dressing (Smith & Nephew) **Study date/s:** February 2013 to April 2016
Outcomes	• SSI • reoperation • pain **Validity of measure/s:** CDC definitions and criteria for superficial, deep, and organ/space SSI were used for the primary outcome. A visual analogue scale was used to assess pain. **Time points:** day 4 and day 30 postsurgery
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation codes were generated on www.randomization.com.
Allocation concealment (selection bias)	Unclear risk	Allocation was performed using a "closed envelope method".
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "the ... study assessor was a senior member of the operating surgical team. The study assessor was not blinded to the treatment group"
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 participant was removed from the intervention arm for a protocol violation, but ITT analysis was provided.
Selective reporting (reporting bias)	Low risk	Expected outcomes reported, but the study protocol was published after the completion of the trial.
Other bias	Low risk	No other bias identified.

Pachowsky 2012

Methods	**Study design:** randomised controlled trial **Ethics and informed consent:** ethics approved and consent obtained. **Sample size calculation:** no **ITT analysis:** yes **number randomised:** 19 **number analysed:** 19 **Follow-up period:** 10 days

Pachowsky 2012 *(Continued)*

	Funding: support received from Smith & Nephew. The authors were responsible for trial design, data analysis, and manuscript writing. The decision to publish trial results was made between study authors and study sponsors. **Pre-registration:** no
Participants	**Location:** University Hospital Erlangen, Germany **Intervention group:** n = 9**control group:** n = 10 **Mean age: intervention group** = 66.2 years (SD 17.83)**control group** = 70.0 years (SD 11.01) **Inclusion criteria:** "consecutive patients who were scheduled for a total hip arthroplasty (THA) for osteoarthritis of the hip were randomised" **Exclusion criteria:** not stated
Interventions	**Aim/s:** to evaluate the use of NPWT to improve wound healing after total hip arthroplasty **Intervention/s in both groups:** "the surgical intervention was identical for both groups. All patients received two Redon drains, one in the deep area of the wound close to the prostheses and one above the closed fascia. The postoperative physiotherapy and mobilisation was also identical for both groups. Both groups received perioperative prophylaxis with antibiotics either Augmentin (amoxicillin trihydrate with potassium clavulanate) or ciprofloxacin" **Group 1 (NPWT) intervention:** "the NPWT group was treated with a PREVENA™ system (KCI, San Antonio, USA). The PREVENA system was left on the wound for five days including the day of surgery" **Group 2 control:** the control group received "the standard wound dressing of our department, consisting of a dry wound coverage". **Study date/s:** not stated
Outcomes	• incidence of seroma (by ultrasound) • amount of wound drainage in the Redon drain canisters • duration of prophylactic antibiotics • secretion from the wound **Validity of measure/s:** "all patients underwent an ultrasound (Zonare, Z.one Ultra SP 4.2, Erlangen, ZONARE Medical Systems, Inc., Mountain View, USA) of the wound" **Time points:** day 5 and day 10 of postoperative period
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes

Pachowsky 2012 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Dressings were left in place for 5 days. The ultrasound was performed on day 5. It was unclear if the person performing the ultrasound was aware of the group to which the participant had been allocated.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All enrolled participants were accounted for in the analyses.
Selective reporting (reporting bias)	Low risk	Results for outcomes identified in the methods section were reported. We did not see the original protocol.
Other bias	High risk	**Evidence:** quote: "Matthias H. Brem gave scientific presentations for KCI. The PREVENA wound treatment system was provided by KCI free of charge". Support was received from Smith & Nephew. The authors were responsible for trial design, data analysis, and manuscript writing. The decision to publish trial results was made between study authors and study sponsors. 1 participant in the NPWT group removed the Redon drain by himself on the first postoperative day.

Pauser 2016

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Sample size estimate:** no **Follow-up period:** 10 days **ITT analysis:** yes **number randomised:** 21 **number analysed:** 21 **Funding:** "Prevena wound treatment system was provided by KCI free of charge" **Pre-registration:** no
Participants	**Location:** Nuremberg, Germany **Intervention group:** n = 11**control group:** n = 10 **Mean age: intervention group** = 81.6 ± 5.2 years**control group** = 82.6 ± 8.6 years **Inclusion criteria:** patients with femoral neck fracture who were scheduled for hip hemiarthroplasty **Exclusion criteria:** not stated
Interventions	**Aim/s:** "to evaluate different aspects of wound healing after fractures of the femoral neck treated by hemiarthroplasty" **Group 1 (NPWT) intervention:** the iNPWT group was treated with a PREVENA system (KCI, San Antonio, Texas). The PREVENA system was left on the wound for 5 days including the day of surgery. **Group 2 control:** control group received the standard wound dressing of our department, consisting of a dry wound coverage (compresses attached to the skin). **Study date/s:** not reported
Outcomes	• seroma **Validity of measure/s:** ultrasound was used as a standardised imaging modality to detect seromas in the wound area.

Pauser 2016 *(Continued)*

	Time points: day 5 and day 10 after surgery
Notes	Investigator contacted for additional details.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information given.
Allocation concealment (selection bias)	Unclear risk	Insufficient information given.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information given.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All those recruited appear to have been included in the analysis.
Selective reporting (reporting bias)	High risk	Only seroma was reported, not SSI.
Other bias	Unclear risk	Data for the NPWT group reported at day 5 and day 10, but data for the control group only reported overall.

Pleger 2018

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Sample size estimate:** no **Follow-up period:** 30 days postoperatively **ITT analysis:** yes **number randomised:** 129 groin incisions (100 participants) **number analysed:** 129 incisions **Funding:** "funded by our own department, without any financial or scientific involvement or support from KCI, ACELITY Company" **Pre-registration:** no
Participants	**Location:** Germany **Intervention group:** n = 58 incisions**control group:** n = 71 incisions

Pleger 2018 *(Continued)*

	Mean age: intervention group = 71 (range 54 to 89)**control group** = 66.5 (range 41 to 86) **Inclusion criteria:** vascular procedures with access to the common femoral artery with at least 1 of the known main risk factors of wound healing: age > 50 years, diabetes mellitus, renal insufficiency, malnutrition, obesity, and chronic obstructive pulmonary disease **Exclusion criteria:** not stated
Interventions	**Aim/s:** to investigate the effectiveness of ciNPT compared with conventional therapy with regard to the incidence of groin WHC on postoperative days 5 to 7 and 30 and the incidence of surgery revisions 30 days postoperatively after various vascular surgeries **Group 1 (NPWT) intervention:** ciNPT applied for postoperative days 5 to 7 **Group 2 (control) intervention:** a conventional adhesive plaster that was changed daily **Study date/s:** 1 February to 30 October 2015
Outcomes	• wound complications **Validity of measure/s:** Szilagyi classification **Time points:** the first evaluation took place on postoperative days 5 to 7 during the hospital stay, while the second evaluation was conducted on postoperative day 30 in the outpatient clinic.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information given.
Allocation concealment (selection bias)	Unclear risk	Insufficient information given.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All those recruited appear to have been included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Results for outcomes identified in the methods section were reported. We did not see the original protocol.
Other bias	High risk	Unequal number of participants in each group; results reported per fracture, so there is a potential unit of analysis issue

Ruhstaller 2017

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** not reported **Follow-up period:** not reported **Sample size estimate:** not reported **ITT analysis:** yes **number randomised:** 136 **number analysed**: not stated **Funding:** KCI collaborated in the trial. **Pre-registration:** yes
Participants	**Location:** Philadelphia, USA **Intervention group:** n = 67**control group:** n = 69 **Mean age:** not reported **Inclusion criteria:** BMI greater than or equal to 30 kg/m^2 at less than or equal to 22 weeks of gestation; woman is labouring; woman is having an unplanned caesarean section; woman will have Pfannenstiel skin incision; has the ability to take a picture and email it to a secure account; receives prenatal care in the University of Pennsylvania health system and plans to follow up postpartum in the system; is 18 years of age or older **Exclusion criteria:** woman cannot read or speak English; is not 18 years of age or older; does not have ability to send a picture by email; has pre-existing diabetes mellitus (type 1 or type 2), is using chronic steroids or immunosuppressants, OR is being actively treated for a malignancy; woman is undergoing a scheduled caesarean section; woman is allergic to silver
Interventions	**Aim/s:** to determine whether NPWT lowers the rate of wound complications in obese pregnant women undergoing an unscheduled intrapartum caesarean section **Group 1 (NPWT) intervention:** NPWT device (PREVENA Incision Management System; Acelity) **Group 2 control:** standard postcaesarean wound care (not defined) **Study date/s:** not stated

Outcomes	Planned outcomes:
	
	• primary outcome variable is wound complications defined as:
	  * any readmission for a wound issue within 4 weeks of discharge;
	  * infection;
	  * wound breakdown.
	• quality of life
	
	Reported outcomes:
	
	• SSI
	• blisters
	• reoperation
	
	Validity of measure/s: not reported
	
	Time points: 4 weeks postsurgery

Notes	Only the abstract and CTR report were available at the time of preparation of this review. Investigator contacted for additional details.

Risk of bias

Bias	Authors' judgement	Support for judgement

Ruhstaller 2017 *(Continued)*

Random sequence generation (selection bias)	Low risk	Once decision for caesarean delivery was established, randomisation was performed using a computer-generated randomisation scheme (Research Electronic Data Capture (REDCap)).
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	**Intervention group:** n = 61/67 (91%);**control group:** n = 58/69 (84%). It was unclear from the abstract if reasons for loss to follow-up were similar across groups.
Selective reporting (reporting bias)	Low risk	Results for outcomes identified in the methods section were reported.
Other bias	Low risk	No other bias identified.

Sabat 2016

Methods	**Study design:** 1:1 parallel-group randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Sample size estimate:** no **Follow-up period:** 4 months **ITT analysis:** no **Funding:** not stated **Pre-registration:** not stated
Participants	**Location:** Philadelphia, USA **Intervention group:** n = 33 wounds**control group:** n = 30 wounds (total 49 participants) **Mean age:** not reported **Inclusion criteria:** people undergoing open vascular surgery involving a groin incision **Exclusion criteria:** not stated
Interventions	**Aim/s:** to compare the effect of postoperative negative pressure therapy to conventional dressings on wound occurrences **Group 1 (NPWT) intervention:** NPWT device **Group 2 control:** conventional dressing (gauze and Tegaderm)

Sabat 2016 *(Continued)*

	Study date/s: not stated
Outcomes	• SSI • wound dehiscence
Notes	Abstract only; unit analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All those recruited appear to have been included in the analysis.
Selective reporting (reporting bias)	Unclear risk	Results for outcomes identified in the methods section were reported. We did not see the original protocol.
Other bias	High risk	Unit analysis

Shen 2017

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** yes **Sample size estimate:** yes (based on a real SSI reduction of 6% from 17% to 11%) **Follow-up period:** 30 days **ITT analysis:** yes **number randomised:** 375 **number analysed**: 265 **Funding:** non-industry **Pre-registration:** yes
Participants	**Location:** Wake Forest University Health Sciences, North Carolina, USA **Intervention group:** n = 187**control group:** n = 188

Shen 2017 *(Continued)*

	Median age (range): intervention group = 59.5 (25 to 85)**control group** = 62 (30 to 81) **Inclusion criteria:** patients who underwent open resection of intra-abdominal neoplasms, where the scheduled procedure was to be performed via midline laparotomy and was a clean-contaminated (class II) case (includes gastric, small bowel, and colorectal resections, as well as bile or pancreatic duct transections); the patient had the ability to understand and the willingness to sign a written informed consent document (either directly or via a legally authorised representative) **Exclusion criteria:** emergent cases; pregnant patients; clean (class I), contaminated (class III), and dirty (class IV) procedures; patients on chronic immunosuppressive medications, including steroids, within the past 3 months; patients with a history of skin allergy to iodine or adhesive drapes were not included in the study
Interventions	**Aim/s:** to decrease the incidence of superficial and deep SSIs **Group 1 (NPWT) intervention:** PICO dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days, or longer if drainage continued, unless soiled or dislodged. **Group 2 control:** Comfeel dressing applied over the primarily closed incision by the surgeon in the operating room. Dressing was left on for 4 days, or longer if drainage continued, unless soiled or dislodged. **Study date/s:** July 2012 to April 2014
Outcomes	• SSI • seroma • haematoma • incisional cellulitis • dehiscence • wound opening for any reason **Validity of measure/s:** CDC definitions for SSI were used. **Time points:** 30 days after surgery
Notes	Investigator contacted for additional details.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "the program nQuery was used to create the randomization schema". The study used permuted-block randomisation with varying block sizes.
Allocation concealment (selection bias)	Low risk	Quote: "an email was sent the day before surgery to the attending surgeon about to which treatment arm the patient had been assigned" **Comment:** notified after randomisation, so probably OK
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	High risk	Investigator team assessed outcomes.

Shen 2017 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Approximately 30% of participants were lost to follow-up or excluded from each arm of the trial. However, reasons for losses were similar between groups. NPWT group: 2 died and 19 were reoperated; standard care group: 5 died and 16 were reoperated
Selective reporting (reporting bias)	Low risk	Prospectively reported. Outcomes were consistent with proposal (National Cancer Institute CCSG P30CA012197).
Other bias	Low risk	No other bias identified.

Stannard 2012

Methods	**Study design:** multicentre randomised controlled trial (4 level 1 trauma centres) **Ethics and informed consent:** ethics approved and consent obtained **Sample size calculation:** no **Follow-up period:** not reported **ITT analysis:** wounds, not people were assessed **Funding:** "funds from corporate/industry were received from Kinetic Concepts, Inc to support this work"
Participants	**Location:** Columbus, Ohio, USA **Intervention group:** n = 130 participants; 141 fractures**control group:** n = 119 participants; 122 fractures **Mean age:** not stated **Inclusion criteria:** people > 18 years of age who had sustained a high-energy tibial plateau, pilon, or calcaneus fracture and were able to comply with research protocol and willing to give informed consent **Exclusion criteria:** non-operative calcaneus, tibia plateau, or pilon fractures; patients with open calcaneus fractures; tibial plateau or calcaneus fractures receiving definitive surgery more than 16 days after injury; pilon fractures receiving definitive surgery more than 21 days after injury; prisoners; pregnant women; patients with one of these fractures as a result of a low-energy mechanism of injury; patients or family members unable or unwilling to sign study informed consent; and patients unable to comply with the protocol
Interventions	**Aim/s:** "to investigate the use of NPWT to prevent wound dehiscence and infection after high-risk lower extremity trauma" **Intervention/s in both groups:** dressings or NPWT were applied in the operating room and then changed on postoperative day 2 and every 1 to 2 days thereafter. **Group 1 (NPWT) intervention:** NPWT over the surgical incision after open reduction and internal fixation of the fracture **Group 2 (control) intervention:** standard postoperative dressing (dressing not described) **Study date/s:** not stated
Outcomes	• wound infection and dehiscence • time to discharge from hospital **Validity of measure/s:** "all infections were confirmed with cultures" **Time points:** not stated - unclear for how long participants were followed up
Notes	

Stannard 2012 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	**Evidence:** quote: "patients were enrolled and then randomised to receive either standard postoperative dressings (control) or NPWT (study)" **Comment:** additional author information: "the randomization was done via a computer generated randomization program"
Allocation concealment (selection bias)	Unclear risk	**Comment:** method not clarified.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	**Evidence:** quote: "a patient was diagnosed as having an infection when a combination of clinical signs and symptoms (purulent drainage, erythema, fever, chills, etc) and laboratory data documented the infection. All infections were confirmed with cultures. Wound dehiscence was defined as any separation of the surgical incision that required either local wound care or surgical treatment" **Comment:** not clear whether those assessing outcomes were aware of group assignment
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	**Comment:** a total of 249 participants were recruited. The same number of participants were reported for both acute and long-term follow-up (follow-up period not defined). Given that 4 hospitals were involved in the study, it seems unusual that complete follow-up would have occurred, suggesting that an available-case analysis may have been performed.
Selective reporting (reporting bias)	Low risk	**Comment:** registered in CTR (NCT00582998) 9 months after final data collection date, so it is unclear whether reported outcomes match the original protocol. However, infection and dehiscence were the expected outcomes.
Other bias	High risk	**Comment:** • unequal number of participants in each group • appears from the protocol that data collection was over many years, but no dates or explanation in manuscript • results reported per fracture, so there is a potential unit of analysis issue

Tanaydin 2018

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics and informed consent:** ethics approved and consent obtained **Sample size calculation:** no **Follow-up period:** 365 days postsurgery

Tanaydin 2018 *(Continued)*

	ITT analysis: wounds (breasts), not people were assessed **Funding:** funded by Smith & Nephew Ltd, who provided the PICO dressings and the Cutometer and financed a research assistant for carrying out the assessments and measurements
Participants	**Location:** the Netherlands **Intervention group:** n = 32**control group:** n = 32 (participants served as their own control) **Mean age (range):** 40.9 (18 to 61) **Inclusion criteria:** patients > 18 years of age who underwent bilateral superomedial pedicle Wise-pattern breast reduction mammoplasty and had postsurgical incisions of similar length on each breast **Exclusion criteria:** pregnancy or lactation, using steroids, or other immune modulators known to affect wound healing; history of radiation of the breast; tattoos in the area of the incision; skin conditions such as cutis laxa that would result in poor healing or widen scars, history of radiation of the breast, patients with a known significant history of hypertrophic scarring or keloids, and postsurgical incisions still actively bleeding, exposure of blood vessels, organs, bone, or tendon at the base of the reference wound; and incisions > 12 inches (30 cm) maximum linear dimension
Interventions	**Aim/s:** to evaluate the effectiveness of postsurgery incision treatment comparing a portable disposable NPWT system with standard care using fixation strips **Group 1 (NPWT) intervention:** a single-use NPWT system without an exudate canister **Group 2 (control) intervention:** fixation strips (Steri-Strip; 3M, St Paul, Minnesota, USA) **Study date/s:** 1 June 2012 to 9 April 2014
Outcomes	• the number of wound-healing complications within 21 days • aesthetic appearance and quality of scarring (additional measurements at 42, 90, 180, and 365 days) **Validity of measure/s:** wound-healing complications were defined as delayed healing (surgical incision not 100% closed at day 7 postsurgery), or occurrence of dehiscence or infection within 21 days postsurgery. **Time points:** all included participants (N = 32) had follow-up visits and assessments at screening (presurgery), day 0 (baseline, postsurgery), day 7, 21, 42, 90, 180, and 365 postsurgery
Notes	The breasts were randomised and served as own control.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation was used for allocation of NPWT and fixation strip to the right or left breast incision site per participant, using sealed envelopes.
Allocation concealment (selection bias)	Unclear risk	Randomisation was used for allocation of NPWT and fixation strip to the right or left breast incision site per participant, using sealed envelopes.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "as NPWT and fixation strips are optically different, blinding of the physician and patients was not feasible; however, data analysis was performed blinded"

Tanaydin 2018 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	32 enrolled participants were accounted for in the analyses.
Selective reporting (reporting bias)	Low risk	Expected outcomes reported. Protocol retrospectively registered as NL40698.068.12/METC12-3-026.
Other bias	Unclear risk	This was a 'split-body' or 'intra-individual' design where a person with 2 wounds had 1 wound randomised to each treatment. It was not clear whether the analysis took this into account.

Tuuli 2017

Methods	**Study design:** randomised controlled trial (abstract only available) **Study grouping:** parallel **Ethics and informed consent:** not recorded **Sample size estimate:** not recorded **Follow-up period:** 30 days **ITT analysis:** yes **number randomised:** 120 **number analysed:** 120 **Funding:** non-industry **Pre-registration:** yes (NCT02578745). Registered 11 June 2012
Participants	**Location:** St Louis, Missouri, USA **Intervention group:** n = 60**control group:** n = 60 **Mean age:** not recorded **Inclusion criteria:** • gestational age ≥ 23 weeks • BMI ≥ 30 at the time of delivery • planned or unplanned caesarean delivery (procedure in which NPWT is being tested) **Exclusion criteria:** • not available for postoperative follow-up • contraindication to NPWT applicable to women undergoing caesarean: pre-existing infection around incision site, bleeding disorder, therapeutic anticoagulation, allergy to any component of the dressing (e.g. silicone, adhesive tape)
Interventions	**Aim/s:** to assess the feasibility of a definitive RCT to test the effectiveness and safety of prophylactic NPWT in obese women after caesarean section **Group 1 (NPWT) intervention:** prophylactic NPWT with the PICO device (Smith & Nephew). Removed at discharge (usually on day 4) **Group 2 (control) intervention:** standard wound dressing (routine postoperative wound dressing consisting of layers of gauze and adhesive tape). The dressing was removed 24 to 48 hours. **Study date/s:** October 2016 to March 2016
Outcomes	• **Primary outcome/s:** composite of superficial or deep surgical site infection; wound separation ≥ 2 cm; SSI; haematoma; seroma • **Secondary outcome/s:** pain score on postoperative day 2 and skin reactions

Tuuli 2017 *(Continued)*

	Validity of measure/s: wound infection defined by CDC criteria (information extracted from CTR) **Time points:** 30 days
Notes	Investigator contacted for additional details.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information in abstract to permit judgement.
Allocation concealment (selection bias)	Unclear risk	Insufficient information in abstract to permit judgement.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information in abstract to permit judgement.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Abstract indicated that 120 participants were randomised and 120 analysed. This was consistent with the number proposed in NCT02578745.
Selective reporting (reporting bias)	Low risk	Reporting was consistent with outcomes proposed in NCT02578745.
Other bias	Unclear risk	None detected. Independently funded trial, however no baseline data presented

Witt-Majchrzac 2015

Methods	**Study design:** randomised controlled trial **Study grouping:** parallel **Ethics** yes **and informed consent:** not stated **Follow-up period:** 6 weeks **Sample size estimate:** no **ITT analysis:** yes **number randomised:** 80 **number analysed:** 80 **Funding:** not stated **Pre-registration:** no
Participants	**Location:** Olsztyn, Poland **Intervention group:** n = 40**control group:** n = 40 **Mean age: intervention group** = 66.2 (± 8), 53 to 80**control group** = 62.1 (± 9.1), 41 to 78

Witt-Majchrzac 2015 *(Continued)*

	Inclusion criteria: patients who underwent an off-pump coronary artery bypass grafting procedure, using the internal mammary artery **Exclusion criteria:** not stated
Interventions	**Aim/s:** not stated **Group 1 (NPWT) intervention:** primary closure with NPWT (PICO, Smith & Nephew) using continuous negative pressure of −80 mmHg. Dressing changed on day 2 or 3 and on day 5 or 6 after surgery. **Group 2 control:** conventional dressings were applied after closure. Dressings changed daily. **Study date/s:** not stated
Outcomes	**Primary outcome/s:** surgical site infection **Secondary outcome/s:** dehiscence, blisters, reoperation
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Authors state only that participants were randomised, without describing method of randomisation.
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	**Evidence for participants:** not possible **Comment:** unlikely to affect outcomes **Evidence for personnel:** not possible **Comment:** unlikely to affect outcomes
Blinding of outcome assessment (detection bias) All outcomes	High risk	Who assessed the outcomes is not stated.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	It is unusual that with a 6-week follow-up there was no attrition in either arm of the trial.
Selective reporting (reporting bias)	Low risk	While no study protocol is available, outcomes identified in the aims are reported (although it is unclear if the authors may have a priori identified other outcomes that were not reported on).
Other bias	Unclear risk	Baseline imbalance in age; NPWT group was older

Abbreviations
ASA: American Society of Anesthesiologists
BMI: body mass index
CABG: coronary artery bypass graft
CDC: US Centers for Disease Control and Prevention
CHEERS: Checklist for Economic Evaluation for Health Interventions
ciNPT: closed incision negative pressure therapy
CS: caesarean section
CTR: clinical trials registry
DVT: deep venous thrombosis

GSV: great saphenous vein
iNPWT: incisional negative pressure wound therapy
IQR: interquartile range
ITT: intention-to-treat
LOS: length of stay
NPC: negative pressure closure
NPD: negative pressure device
NPWT: negative pressure wound therapy
OR: operating room (theatre)
ORIF: open reduction and internal fixation surgery
PCA: patient-controlled analgesia
PP analysis: per-protocol
QoL: quality of life
RCT: randomised controlled trial
SAWT: subatmospheric pressure wound therapy system
SD: standard deviation
SF-12: 12-item Short Form Health Survey
SPD: static pressure dressing
SPID: sum of pain intensity differences
SSI: surgical site infection
SSO: surgical site occurrence
THA: total hip arthroplasty
TKR: total knee replacement
TKA: total knee arthroplasty
VAC: vacuum-assisted closure
WHC: wound-healing complication

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Al-Inany 2002	Wrong intervention
Albert 2012	No acute wounds were included.
Anderson 2014	Feasibility study. Predefined criteria used to assess feasibility included: recruitment (> 75% participation); loss to follow-up (< 10%); intervention fidelity (= 95%); and interrater reliability (kappa = 0.8). Assessment of clinical outcomes was not planned or conducted.
Banasiewicz 2013	Included infected wounds
Bondokji 2011	Prospective cohort study
Braakenburg 2006	Chronic and acute wounds were reported together, and further information was not available.
Chiang 2017	Open wounds
Chio 2010	Skin graft study
Dorafshar 2012	The study used NPWT to treat existing non-healing skin graft wounds.
Eisenhardt 2012	Skin graft study; no inclusion of wounds healing by primary closure
Grauhan 2013	Quasi-randomised study: "A total of 156 patients were enrolled and allocated to 2 study groups, alternating according to the time of operation"
Hu 2009	Acute, subacute, and chronic wounds were included. Acute wounds were defined as those that had been "open" for less than 1 week.

Study	Reason for exclusion
Johannesson 2008	The intervention dressing was not a continuous negative pressure device.
Kim 2007	The study was not a randomised controlled trial.
Li 2016	Quasi-randomisation (by odd and even numbers)
Llanos 2006	Skin graft study
Moisidis 2004	Skin graft study; no inclusion of wounds healing by primary closure
Mouës 2004	No inclusion of acute wounds
Mouës 2007	No inclusion of acute wounds
Pellino 2014	Non-randomised study in people with Crohn's disease
Petkar 2012	Skin graft study
Rahmanian-Schwarz 2012	Included chronic and acute wounds, and these were not separately reported
Visser 2017	The vacuum therapy device was a syringe inserted subcutaneously into the dressing, which was used to create a vacuum. Consequently, it was not a standard, continuous pressure device.
Yu 2017	A drain was left inside the wound, so not strictly a primarily closed wound.

NPWT: negative pressure wound therapy

Characteristics of studies awaiting assessment *[ordered by study ID]*

NCT00654641

Methods	Randomised controlled trial
Participants	Obese women undergoing caesarean delivery
Interventions	Negative pressure wound therapy versus standard wound closure
Outcomes	Total number of women experiencing a wound complication
Notes	

NCT00724750

Methods	Randomised controlled trial
Participants	Hospitalised patients with acute wounds resulting from either trauma, dehiscence, or surgical complications
Interventions	Gauze suction (G-SUC) negative pressure wound therapy versus vacuum-assisted closure device (VAC) negative pressure wound therapy
Outcomes	Per cent change per day in wound surface area; per cent change per day in wound volume

NCT00724750 *(Continued)*

Notes	

NCT02064270

Methods	Randomised controlled trial
Participants	Patient is scheduled to have a surgical procedure for total knee arthroplasty or total hip arthroplasty (primary or revision procedure).
Interventions	Negative pressure wound therapy versus standard postsurgical dressings
Outcomes	Incision appearance based on VAS; drainage amount; user-friendliness for patient; number of participants with complications; return to the operating room; need for antibiotics
Notes	

NCT02127281

Methods	Randomised controlled trial
Participants	Patients with a scheduled revision total hip or knee arthroplasty procedure
Interventions	PREVENA versus control
Outcomes	Number of participants with wound complications; reoperation rates; readmission rates; knee flexion; HOOS and KOOS scores at 90 days postoperatively; timed-up-and-go test; hip range of motion (flexion); VR-12 questionnaire; hip range of motion; knee extension
Notes	

NCT02147288

Methods	Randomised controlled trial
Participants	Patients undergoing panniculectomy, formal abdominoplasty, formal lipo-abdominoplasty, ventral hernia repair using acellular dermal matrix, bilateral breast reconstruction
Interventions	Renasys*GO negative pressure wound therapy system versus standard care
Outcomes	Postoperative seroma formation
Notes	

HOOS: hip disability and osteoarthritis outcome score
KOOS: knee disability and osteoarthritis outcome score
VAS: visual analogue scale
VR-12: Veterans RAND 12-Item Health Survey

Characteristics of ongoing studies *[ordered by study ID]*

ACTRN12612000550808	
Trial name or title	Pilot study of negative pressure wound dressing therapy versus standard care dressing to prevent surgical site infection in patient undergoing hip arthroplasty
Methods	Randomised controlled trial
Participants	Patients booked for primary hip arthroplasty
Interventions	Negative pressure wound therapy versus standard wound dressing
Outcomes	Presence of surgical site infection; wound complications including dehiscence, haematoma, and seroma will be assessed by visual inspection; hospital readmission
Starting date	2012
Contact information	b.gillespie@griffith.edu.au
Notes	

ACTRN12612001275853	
Trial name or title	Effectiveness of negative pressure wound therapy (NPWT) in the prevention of post-operative surgical wound dehiscence in at risk patients following abdominal surgery; a multicentre randomised control trial
Methods	Randomised controlled trial
Participants	Patients undergoing an abdominal surgical procedure that uses a midline laparotomy as the surgical entry
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Occurrence of surgical wound dehiscence; occurrence of surgical site infection
Starting date	2012
Contact information	kylie.sandy-hodgetts@curtin.edu.au
Notes	

ACTRN12615000175572	
Trial name or title	Do suction assisted negative pressure dressings reduce the incidence of surgical site infections after abdominal surgery: a randomized controlled trial
Methods	Randomised controlled trial
Participants	Patients undergoing laparotomy (where abdominal incision breaches peritoneum, and wound is large enough to at least fit the surgeon's hand)
Interventions	Negative pressure wound therapy versus standard dressing used with a clear film with an absorbent layer

ACTRN12615000175572 *(Continued)*

Outcomes	Wound infection; patient satisfaction
Starting date	2015
Contact information	peeyau.tan@monashhealth.org
Notes	

ACTRN12615000286549

Trial name or title	Negative pressure wound therapy versus standard care dressing to prevent surgical site infections in obese women undergoing caesarean section
Methods	Randomised controlled trial
Participants	Obese women following caesarean section
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Presence of SSI; wound complications; hospital readmissions; hospital length of stay; QoL
Starting date	2015
Contact information	b.gillespie@griffith.edu.au
Notes	

ACTRN12615001350516

Trial name or title	Negative pressure wound therapy (NPWT) versus conventional wound dressings in total knee arthroplasty
Methods	Randomised controlled trial
Participants	Patients undergoing total knee arthroplasty for treatment of knee arthritis
Interventions	Negative pressure wound therapy versus conventional dressings
Outcomes	Cost of dressings changes; patient satisfaction; patient preference; patient morbidity assessment
Starting date	Unknown
Contact information	research_coordinator@oriql.com.au
Notes	

ACTRN12618000026224p

Trial name or title	Effect of negative pressure dressing versus standard wound dressing on the rate of wound dehiscence in patients undergoing pilonidal surgery

ACTRN12618000026224p *(Continued)*

Methods	Randomised controlled trial
Participants	Patients undergoing pilonidal surgery
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Rate of wound dehiscence; time taken for the wound to fully heal; rate of disease recurrence; analgesia requirements for the wound; ratio of wound size; patient satisfaction 2 months postoperatively; QoL
Starting date	2017
Contact information	Ram.Nataraja@monashhealth.org
Notes	

ChiCTR -IOR-15006439

Trial name or title	Prevention surgical site infection with using negative pressure wound therapy in abdominal incision
Methods	Parallel randomised controlled trial
Participants	High-risk patients: including abdominal surgery for malignancy, colorectal, abdominal wall reconstruction
Interventions	Negative pressure wound therapy versus routine approach
Outcomes	Rate of surgical site infection
Starting date	2015
Contact information	hpzhangly@163.com
Notes	

DRKS00006199

Trial name or title	Postoperative negative pressure incision therapy following open colorectal surgery: a randomized-controlled trial
Methods	Randomised controlled trial
Participants	Patients undergoing planned elective open colorectal surgery via median or transverse laparotomy
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Rate of SSI; length of hospital stay; rate of reoperations; rate of antibiotic therapy; duration of postoperative negative pressure incision therapy (intervention arm only); wound pain assessed with VAS; rate of wound complications other than wound infections; rate of serious adverse events
Starting date	1 October 2015

DRKS00006199 *(Continued)*

Contact information	Unclear
Notes	

DRKS00011033

Trial name or title	Evaluation of negative pressure incisional therapy in urgent gastro-intestinal surgery for reduction of superficial surgical site infections compared to non-occlusive conventional plaster - a prospective, randomized, controlled, multicenter clinical trial
Methods	Randomised controlled trial
Participants	Patients undergoing urgent laparotomy due to an acute gastrointestinal disorder
Interventions	Negative pressure wound therapy versus non-occlusive conventional plaster
Outcomes	SSI; prolongation of hospitalisation due to SSI; cosmetic result; safety endpoints: AEs, SAEs
Starting date	21 September 2016
Contact information	Unclear
Notes	

ISRCTN12702354

Trial name or title	Wound healing in surgical trauma
Methods	Randomised controlled trial
Participants	Major trauma patients aged 16 years or over requiring surgery to treat a broken leg
Interventions	Negative pressure wound therapy versus standard-of-care wound dressing
Outcomes	Deep infection rate; QoL; wound healing; number and nature of further surgical interventions; cost-effectiveness; long-term disability; chronic neuropathic pain
Starting date	January 2016
Contact information	WHIST@ndorms.ox.ac.uk
Notes	

ISRCTN31224450

Trial name or title	Negative pressure therapy in large incisional hernia surgery
Methods	Randomised controlled trial (case-control)
Participants	Patients undergoing elective surgery for incisional hernia with diameters exceeding 10 cm

ISRCTN31224450 *(Continued)*

Interventions	Negative pressure wound therapy versus traditional dressing
Outcomes	**Primary:** volume accumulated in the drains every 24 hours in millilitres; number of days needed to reduce this volume under 50 mL per 24 hours **Secondary:** postoperative complications; cost
Starting date	1 February 2013
Contact information	drcarlesolona@gmail.com
Notes	

ISRCTN55305726

Trial name or title	WHITE 7 - WHISH – wound healing in surgery for hip fractures
Methods	Randomised controlled trial
Participants	Adults aged 65 years or older with a hip fracture that requires surgery
Interventions	Negative pressure wound therapy versus standard wound dressing
Outcomes	Deep infection; mortality rate; QoL; complications and surgical interventions; cost consequences and resource use; mobility; residential status; recruitment rate; retention rate
Starting date	1 March 2017
Contact information	lucy.sansom@ndorms.ox.ac.uk
Notes	

ISRCTN92903493

Trial name or title	Post-operative wound management
Methods	Randomised controlled trial
Participants	Patients undergoing primary total hip or knee replacement
Interventions	Negative pressure wound therapy versus standard wound dressing
Outcomes	No outcomes are listed in the trial registration record. For primary outcomes it states " To introduce a new postoperative wound management protocol based on using PICO NPWT"
Starting date	16 August 2012
Contact information	sudheer.karlakki@rjah.nhs.uk
Notes	

NCT01450631

Trial name or title	The use of the Prevena incision management system on post-surgical cesarean section incisions
Methods	Randomised controlled trial
Participants	Patients undergoing caesarean section procedures using a subcuticular skin closure technique within the next 42 days
Interventions	PREVENA Incision Management System versus standard-of-care dressing
Outcomes	Incidence of postoperative surgical site occurrences post-caesarean section surgery
Starting date	2011
Contact information	Robert Heine, Duke University
Notes	

NCT01640366

Trial name or title	PICO breast reduction clinical study looking at incision healing complications
Methods	Randomised controlled trial
Participants	Patients undergoing an elective surgical procedure for bilateral reduction mammoplasty
Interventions	PICO negative pressure versus standard-of-care dressing
Outcomes	Difference in incision-healing complications; aesthetic appearance (cosmesis) and scar quality; difference in the amount of skin, nipple, and areola necrosis; difference in the number of haematomas, seromas, infections; difference in the amount of dehiscence
Starting date	2012
Contact information	Robert D Galiano, Northwestern University Feinberg School of Medicine
Notes	

NCT01656044

Trial name or title	Negative pressure therapy in preventing infection after surgery in patients with colon, rectal, pancreatic, or peritoneal surface cancer
Methods	Randomised controlled trial
Participants	Surgical resection for a colorectal, pancreatic, or peritoneal surface malignancy
Interventions	Negative pressure therapy (NPT) versus standard sterile dressing (SSD)
Outcomes	Rate of incisional surgical site infection; rates of organ/space SSIs, seromas, haematomas, incisional cellulitis, and wound opening for any reason; cost of NPT and SSD

NCT01656044 *(Continued)*

Starting date	2012
Contact information	Perry Shen, Wake Forest University Health Sciences
Notes	

NCT01698372

Trial name or title	Negative pressure dressing after saphenous vein harvest
Methods	Randomised controlled trial
Participants	Patients presenting for elective or semi-elective isolated first-time CABG surgery with harvesting of the greater saphenous vein
Interventions	PREVENA device versus conventional dressing
Outcomes	Change from baseline ASEPSIS score of wound healing at 6 weeks; total pain level score
Starting date	2012
Contact information	Paul Fedak, University of Calgary
Notes	

NCT01770067

Trial name or title	Prophylactic treatment of high-risk patients with cardiovascular implantable electronic devices (CIED) with continuous in-situ ultra high-dose antibiotics (CITA) under regulated negative pressure-assisted wound therapy (RNPT)
Methods	Randomised controlled trial
Participants	Patients undergoing cardiovascular implantable electronic devices surgery
Interventions	High-dose antibiotics (CITA) under regulated negative pressure-assisted wound therapy (RNPT) versus CITA
Outcomes	Lack of CIED infection
Starting date	February 2013
Contact information	Unknown
Notes	

NCT01890720

Trial name or title	Incisional negative pressure wound therapy for prevention of postoperative infections following caesarean section

NCT01890720 *(Continued)*

Methods	Randomised controlled trial
Participants	Patients undergoing a caesarean section with a pre-gestational BMI ≥ 30 kg/m^2
Interventions	Negative pressure wound therapy versus standard postoperative wound dressing
Outcomes	The incidence of post-CS wound infection; length of primary and any secondary hospitalisation; readmissions to hospital/contact with general practitioner; decreased health-related quality of life score; antibiotic treatment; cosmetic outcome; other wound complications
Starting date	2013
Contact information	Nana Hyldig, Odense University Hospital
Notes	

NCT01891006

Trial name or title	Intervention for postpartum infections following caesarean section (APIPICS)
Methods	Randomised controlled trial
Participants	Patients 18 years of age or older with postpartum infections following caesarean section
Interventions	Negative pressure wound therapy versus standard wound dressing
Outcomes	Frequency of re-rupture in each study group; length of hospitalisation; readmission to hospital; decreased health-related quality of life score; cosmetic outcome
Starting date	2013
Contact information	Nana Hyldig
Notes	

NCT01905397

Trial name or title	Negative pressure wound therapy to reduce surgical site infection
Methods	Randomised controlled trial
Participants	Scheduled for an elective surgery in either open CRS or open HPBS
Interventions	Negative pressure wound therapy versus conventional wound therapy
Outcomes	Incidence of surgical site infection; characterisation of surgical site infection; length of hospital stay
Starting date	2013
Contact information	Trey Blazer, Duke University
Notes	

NCT01913132

Trial name or title	PICO above incisions after vascular surgery
Methods	Randomised controlled trial
Participants	Patients 18 years of age and above undergoing elective vascular surgery
Interventions	Negative pressure wound therapy with PICO versus standard dressing
Outcomes	Wound infection; cost
Starting date	2013
Contact information	Stefan Acosta, Skåne University Hospital
Notes	

NCT02007018

Trial name or title	Negative pressure wound therapy use to decrease surgical nosocomial events in colorectal resections (NEPTUNE)
Methods	Randomised controlled trial
Participants	Patients undergoing an elective colorectal resection through a midline laparotomy incision
Interventions	Negative pressure wound therapy versus usual care
Outcomes	SSI; need for home nursing care related to SSI; length of hospital stay; cost of management of SSI; number of return visits related to SSI
Starting date	January 2015
Contact information	Unknown
Notes	

NCT02020018

Trial name or title	Negative pressure wound therapy for prevention of poststernotomy infection
Methods	Randomised controlled trial
Participants	Patients undergoing open heart surgery
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Wound infection after open-heart surgery; reoperation for wound infection; length of stay
Starting date	December 2013

NCT02020018 *(Continued)*

Contact information	Unknown
Notes	

NCT02084017

Trial name or title	Negative pressure wound therapy for the prevention of surgical site infection following lower limb revascularization
Methods	Randomised controlled trial
Participants	Patients undergoing surgery to restore blood flow to the lower limb(s)
Interventions	Negative pressure wound therapy versus standard Tegaderm (3M Health Care, St Paul, Minnesota) adhesive dressing
Outcomes	SSI; length of stay; emergency room visits; all-cause mortality; reoperation rate; amputation
Starting date	July 2014
Contact information	Unknown
Notes	

NCT02118558

Trial name or title	Negative pressure wound therapy – PREVENA – in prevention of infections after total knee arthroplasty (TKA)
Methods	Randomised controlled trial
Participants	Patients undergoing knee arthroplasty
Interventions	Negative pressure wound therapy versus standard prophylactic therapy
Outcomes	Proportion of infections; number of participants recommended to undergo further procedural intervention due to infection
Starting date	June 2014
Contact information	Unknown
Notes	

NCT02302222

Trial name or title	The management of closed surgical incisions resulting from incisional hernia repair and/or functional panniculectomy using the Prevena Customizable dressing
Methods	Randomised controlled trial

NCT02302222 *(Continued)*

Participants	Adults undergoing panniculectomy or hernia repair; BMI ≥ 30; preoperatively assessed to undergo a procedure resulting in a clean/clean-contaminated wound
Interventions	PREVENA Customizable Dressing with ACTIV.A.C. therapy unit versus standard dressing
Outcomes	Incidence of SSI or dehiscence within 30 days of surgery; incidence of clinically relevant intervention (antimicrobial treatment, drainage, debridement, reoperation, application of NPWT) within 30 days of surgery
Starting date	2015
Contact information	Not stated
Notes	

NCT02309944

Trial name or title	Negative pressure wound therapy in obese gynecologic oncology patients
Methods	Randomised controlled trial
Participants	Patients undergoing laparotomy for suspected gynecologic malignancy
Interventions	Negative pressure wound therapy versus standard wound management
Outcomes	Rate of wound complications; time from surgery to starting adjuvant therapy among those with confirmed malignancies
Starting date	May 2015
Contact information	mhgerber@umn.edu
Notes	

NCT02331485

Trial name or title	Randomised control study to assess the role of negative pressure wound therapy (NPWT) in the management of wound in surgical patient
Methods	Randomised controlled trial
Participants	Patients undergoing laparotomy with 1 of: high BMI; malignancy; malnutrition; type 2 diabetes; emergency surgery; postradiochemotherapy; steroids; open colorectal resection; and at least 2 of: smoking; age > 75 years; diffuse atherosclerotic disease involving arteries
Interventions	Negative pressure wound therapy (PICO + Acticoat group) versus standard wound management
Outcomes	Reduction in wound infection by 50%; reduction in length of hospital stay; decrease in antibiotic use for wound infection management; decreased cost of patient treatment
Starting date	August 2014

NCT02331485 *(Continued)*

Contact information	mikazanowski@gmail.com; sebastian.smolarek79@gmail.com
Notes	

NCT02348034

Trial name or title	A randomized controlled trial exploring the ability of negative pressure wound therapy (NPWT) to reduce colorectal surgical site infections (SSI)
Methods	Randomised controlled trial
Participants	Patients undergoing elective colorectal surgery
Interventions	PREVENA dressing versus usual care
Outcomes	Presence/absence of superficial surgical site infection; presence/absence of intervention-related side effects
Starting date	November 2015
Contact information	gag511@mail.usask.ca
Notes	

NCT02389023

Trial name or title	Comparison of Prevena negative pressure incision management system vs. standard dressing after vascular surgery
Methods	Randomised controlled trial
Participants	Not stated
Interventions	PREVENA incision management system versus standard gauze dressing
Outcomes	Surgical site infection, major wound non-infectious complications, or graft infection; surgical site infection alone; patient satisfaction; total costs; length of index hospital stay and any readmission; major adverse limb event (MALE) or postoperative death
Starting date	2015
Contact information	daniel.bertges@uvmhealth.edu; lisa.smith@med.uvm.edu
Notes	

NCT02395159

Trial name or title	Reduction of groin wound infections after vascular surgery by using an incision management system (IMS)

NCT02395159 *(Continued)*

Methods	Randomised controlled trial
Participants	Patients undergoing vascular surgery via right or left inguinal approach
Interventions	PREVENA IMS versus sterile plaster dressings
Outcomes	Wound infection; length of hospital stay; revision surgery; necessity of alternative wound dressings; prolongation of ambulant treatment
Starting date	2015
Contact information	Jochen Grommes, Aachen University Hospital
Notes	

NCT02408835

Trial name or title	Negative pressure wound therapy in groin dissection
Methods	Randomised controlled trial
Participants	Patients undergoing inguinal lymphadenectomy for metastatic carcinoma of cutaneous origin
Interventions	Negative pressure wound therapy versus conventional wound care
Outcomes	Time to wound healing; wound infection; lymphoedema; need for further surgical interventions to achieve wound healing; scar appearance; patient-reported outcomes
Starting date	July 2015
Contact information	s.mcallister@qub.ac.uk
Notes	

NCT02492854

Trial name or title	Standard versus PICO dressings in lower-extremity bypass patients (PICO-LEB)
Methods	Randomised controlled trial
Participants	Patients undergoing lower extremity bypass using ipsilateral great saphenous vein harvest
Interventions	PICO single-use negative pressure dressings versus sterile gauze dressings
Outcomes	Infection of surgical site incision; function and quality of life; resource utilisation in dollars
Starting date	2015
Contact information	Jeffrey.Siracuse@bmc.org; twtcheng@bu.edu
Notes	

NCT02509260

Trial name or title	Prevena incisional negative pressure wound therapy in re-operative colorectal surgery
Methods	Randomised controlled trial
Participants	Patients undergoing open reoperative colorectal surgery
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Occurrence of superficial surgical site infection; length of hospital stay; cost-effectiveness; clinical efficacy of the device in relation to the degree of contamination
Starting date	July 2015
Contact information	ASHBURJ@ccf.org
Notes	

NCT02558764

Trial name or title	Effects of preventive negative pressure wound therapy with PICO on surgical wounds of kidney transplant patients
Methods	Randomised controlled trial
Participants	Patients admitted for cadaveric kidney transplant surgery
Interventions	Negative pressure wound therapy versus basic wound contact absorbent dressings
Outcomes	Post-kidney transplant wound complication rates
Starting date	November 2015
Contact information	Unknown
Notes	

NCT02578745

Trial name or title	Prophylactic incisional care in obese women at cesarean (PICO-C)
Methods	Randomised controlled trial
Participants	Patients with planned or unplanned caesarean delivery with a BMI ≥ 30 at the time of delivery
Interventions	Prophylactic NPWT versus standard dressing
Outcomes	Surgical site infection or other wound complications; individual components of composite wound complications; pain score on 0-to-10 scale; positive wound cultures and specific organisms such as MRSA; prophylactic negative pressure-related adverse events including blisters

NCT02578745 *(Continued)*

Starting date	2015
Contact information	Methodius G Tuuli, Washington University School of Medicine
Notes	

NCT02581904

Trial name or title	Prevena vascular groin wound study
Methods	Randomised controlled trial
Participants	All patients undergoing a femoral incision during vascular reconstruction or repair will be considered for study.
Interventions	PREVENA care versus dry gauze dressing care
Outcomes	Groin wound complication; hospital length of stay; return to operating room; hospital readmission; index hospital cost
Starting date	2015
Contact information	Paul DiMuzio, Thomas Jefferson University
Notes	

NCT02664168

Trial name or title	A comparative study to assess the prevention of surgical site infection (SSI's) in revision total joint arthroplasty patients treated with single-use negative pressure wound therapy (PICO) or standard care dressings (AQUACEL Ag surgical dressing)
Methods	Randomised controlled trial
Participants	Patients undergoing revision total knee arthroplasty or revision total hip arthroplasty
Interventions	Single-use negative pressure wound therapy versus AQUACEL Ag Surgical dressing
Outcomes	Incidence of surgical site infection
Starting date	January 2016
Contact information	tiffany.morrison@rothmaninstitute.com
Notes	

NCT02682316

Trial name or title	Negative pressure wound therapy in post-operative incision management

NCT02682316 *(Continued)*

Methods	Randomised controlled trial
Participants	Women of any BMI undergoing a laparotomy procedure for a presumed gynaecologic malignancy, or morbidly obese
Interventions	Negative pressure wound therapy versus usual standard dry gauze
Outcomes	Number of postoperative wound complications
Starting date	February 2016
Contact information	Mario Leitao
Notes	

NCT02780453

Trial name or title	Prophylactic negative pressure dressings for closed laparotomy wounds - a randomised, controlled, open label trial
Methods	Randomised controlled trial
Participants	Patients undergoing elective and emergency abdominal surgery
Interventions	Negative pressure dressing versus standard wound dressing
Outcomes	Surgical site infection rate
Starting date	2016
Contact information	Unknown
Notes	

NCT02790385

Trial name or title	Negative pressure wound therapy - a multi-centered randomized control trial (NPWT)
Methods	Randomised controlled trial
Participants	Patients undergoing posterior spinal surgery categorised as high risk for infection
Interventions	Negative pressure wound therapy versus standard gauze treatment
Outcomes	Wound infection; time for wound closure; cosmetic results; caregiver/parental satisfaction; wound dehiscence; foreign body reaction
Starting date	July 2014
Contact information	Unknown
Notes	

NCT02799667

Trial name or title	Do single use negative pressure dressings reduce wound complications in obese women after cesarean delivery?
Methods	Randomised controlled trial
Participants	Obese women (BMI > 40 kg/m^2) undergoing caesarean delivery
Interventions	Negative pressure wound therapy versus conventional dressing
Outcomes	Presence of wound complications
Starting date	May 2016
Contact information	sbakaysa@tuftsmedicalcenter.org
Notes	

NCT02892435

Trial name or title	Prevena incision management system vs conventional management for wound healing
Methods	Randomised controlled trial
Participants	Patients submitted to contaminated or dirty abdominal surgery
Interventions	Negative pressure wound therapy versus conventional dressing
Outcomes	SSI; reduction in wound complications in participants with associated risk factors (e.g. diabetes, obesity, and cancer)
Starting date	November 2014
Contact information	alessia.garzi@gmail.com
Notes	

NCT02901405

Trial name or title	NPWT in soft tissue sarcoma surgery
Methods	Randomised controlled trial
Participants	Adults undergoing primary soft tissue sarcoma excision that is primarily closed
Interventions	Negative pressure wound therapy versus standard dressings
Outcomes	Surgical site infection; time to wound dryness; delay to discharge from hospital; adverse events; cost analysis
Starting date	2016

NCT02901405 *(Continued)*

Contact information	ashish.mahendra@ggc.scot.nhs.uk
Notes	

NCT02901613

Trial name or title	Prophylactic post-cesarean incisional negative-pressure wound therapy in morbidly obese patients
Methods	Randomised controlled trial
Participants	Morbidly obese patients who have undergone caesarean section
Interventions	Negative pressure wound therapy versus standard dry sterile dressing
Outcomes	Wound complications
Starting date	August 2016
Contact information	denefrc@mail.amc.edu
Notes	

NCT02926924

Trial name or title	Prophylactic application of an incisional wound vac to prevent wound complications in obese spine surgery patients
Methods	Randomised controlled trial
Participants	Patients scheduled to have posterior spine surgery; BMI ≥ 35
Interventions	Wound VAC versus standard dressing
Outcomes	Postoperative infection requiring return to operating room
Starting date	2016
Contact information	jaimeeg@med.umich.edu
Notes	

NCT02954835

Trial name or title	Negative pressure therapy for groin wounds
Methods	Randomised controlled trial
Participants	Patients undergoing vascular surgery with a groin incision
Interventions	PREVENA versus traditional dressing

NCT02954835 *(Continued)*

Outcomes	Infection rate
Starting date	2016
Contact information	thomas.bernik@ehmchealth.org; courtney.woodhull@ehmchealth.org
Notes	

NCT02967627

Trial name or title	VAC dressings for colorectal resections (VACCRR)
Methods	Randomised controlled trial
Participants	Patients undergoing elective colorectal resection for benign or malignant disease
Interventions	Negative pressure wound therapy versus sterile gauze dressing
Outcomes	SSI; wound complication; length of stay; wound-related visits postsurgery; need for and duration of home care; blistering/reaction to wound dressings; postoperative complications
Starting date	November 2016
Contact information	mitchell.webb@alumni.ubc.ca
Notes	

NCT03000010

Trial name or title	Wound Vac bandage comparison after spinal fusion (WV)
Methods	Randomised controlled trial
Participants	Patients with neuromuscular scoliosis undergoing posterior spinal fusion
Interventions	Incisional wound VAC versus normal gauze bandage group
Outcomes	Prevention of wound dehiscence or infection
Starting date	2016
Contact information	mcburke@med.umich.edu
Notes	

NCT03009110

Trial name or title	Preventing adverse incisional outcomes at cesarean multicenter trial (Prevena-C)
Methods	Randomised controlled trial

NCT03009110 *(Continued)*

Participants	Women undergoing planned or unplanned caesarean delivery
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Frequency of superficial or deep surgical site infections
Starting date	February 2017
Contact information	martins@wudosis.wustl.edu
Notes	

NCT03010137

Trial name or title	Incisional negative pressure wound therapy in high risk patients undergoing panniculectomy: a prospective randomized controlled trial
Methods	Randomised controlled trial
Participants	Patients undergoing panniculectomy in preparation for renal transplantation
Interventions	Negative pressure wound therapy versus standard closure
Outcomes	Wound-healing complications; time to drain removal; scarring; pain; QoL
Starting date	December 2015
Contact information	cbailey@ucdavis.edu
Notes	

NCT03021668

Trial name or title	Comparison between wound vacuum dressing and standard closure to reduce rates of surgical site infections
Methods	Randomised controlled trial
Participants	Patient to undergo pancreaticoduodenectomy for pancreatic tumours at the Johns Hopkins Hospital
Interventions	PREVENA Peel & Place dressing versus standard closure of surgical incision
Outcomes	Rate of surgical site infection; prolonged length of stay; rate of readmission; time to adjuvant therapy
Starting date	2017
Contact information	Matthew J Weiss, Johns Hopkins University
Notes	

NCT03061903

Trial name or title	Closed incision negative pressure therapy vs standard care (Prevena)
Methods	Randomised controlled trial
Participants	Patients undergoing primary total hip arthroplasty through a direct anterior approach with: diabetes; obesity (BMI > 30); active smoking; previous hip surgery
Interventions	PREVENA versus AQUACEL
Outcomes	Prevalence of wound complications; duration of wound-healing delay; length of hospital stay; number of days on antibiotic therapy; average cost of wound treatment
Starting date	2017
Contact information	mh3818@cumc.columbia.edu; rs3464@cumc.columbia.edu
Notes	

NCT03069885

Trial name or title	iNPWT in immediate breast reconstruction
Methods	Randomised controlled trial
Participants	Patients admitted for immediate breast reconstruction
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Time to removal of surgical drains; SSI; skin necrosis; hospitalisation time; participant and observer assessment of the scars; patient satisfaction and quality of life
Starting date	November 2017
Contact information	Unknown
Notes	

NCT03082664

Trial name or title	Negative pressure wound therapy to prevent wound complications following cesarean section in high risk patients
Methods	Randomised controlled trial
Participants	Caesarean section in high-risk obstetric patients
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Wound complications: wound breakdown, infection, separation, dehiscence

NCT03082664 *(Continued)*

Starting date	June 2015
Contact information	meghanhill@obgyn.arizona.edu
Notes	

NCT03144726

Trial name or title	RCT on NPWT for incisions following major lower-limb amputation to reduce surgical site infection
Methods	Randomised controlled trial
Participants	Any patient 18 years or older undergoing amputation of the lower limb, either an above-knee amputation or below-knee amputation
Interventions	Negative pressure wound therapy versus standard dressing
Outcomes	Surgical site infection; length of stay; antibiotic use; reoperation; death
Starting date	2017
Contact information	oonagh.scallan@lhsc.on.ca
Notes	

NCT03175718

Trial name or title	INPWT on wound complications & clinical outcomes after lower extremity sarcoma surgery preop radiation therapy patients (VAC)
Methods	Randomised controlled trial
Participants	Patients with lower extremity soft tissue sarcoma confirmed by tissue pathology
Interventions	VAC wound dressing versus wound dressing
Outcomes	Wound complications including reoperation for superficial or deep site infection; quality of life; functional outcome; overall cost
Starting date	2017
Contact information	yalmosuli@ohri.ca; jdobransky@ohri.ca
Notes	

NCT03180346

Trial name or title	A prospective, randomized, comparative study to assess the prevention of surgical site infection (SSI's) in revision total joint arthroplasty patients treated with single-use negative pressure wound therapy (PICO) or standard care dressings (AQUACEL Ag surgical dressing)

NCT03180346 *(Continued)*

Methods	Randomised controlled trial
Participants	Patients undergoing revision total knee arthroplasty or revision total hip arthroplasty
Interventions	Negative pressure wound therapy versus standard care
Outcomes	SSI
Starting date	March 2017
Contact information	Unknown
Notes	

NCT03250442

Trial name or title	Evaluating the outcomes for incisional application of negative pressure for nontraumatic amputations
Methods	Randomised controlled trial
Participants	Patient requires closure of a non-traumatic transmetatarsal amputation, below-knee amputation, knee disarticulation, or above-knee amputation.
Interventions	PREVENA device versus standard dry dressing
Outcomes	Proportion of postoperative incision complications between the 2 arms; length of hospital stay; number of surgically related wound readmissions; Medical Outcomes Study 12-item Short Form Health Survey (SF-12); percentage of closed incisions remaining closed at 1, 2, and 3 months post-hospital discharge
Starting date	2017
Contact information	paul.j.kim@gunet.georgetown.edu
Notes	

NCT03269968

Trial name or title	Use of negative pressure wound therapy in morbidly obese women after cesarean delivery
Methods	Randomised controlled trial
Participants	Obese women undergoing elective caesarean delivery
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Composite wound complication; patient survey
Starting date	October 2017
Contact information	Tetsuya Kawakita (tetsuya.x.kawakita@medstar.net)

NCT03269968 *(Continued)*

Notes	

NCT03274466

Trial name or title	Closed incision negative pressure therapy versus standard of care surgical dressing in revision total knee arthroplasty (PROMISES)
Methods	Randomised controlled trial
Participants	Patient requires a TKA revision defined as: a 1-stage aseptic revision procedure; a 1-stage septic exchange procedure for acute postoperative infection; removal of cement spacer and re-implantation procedure; open reduction and internal fixation of periprosthetic fractures.
Interventions	Closed incision negative pressure therapy (ciNPT) versus standard-of-care dressing
Outcomes	Surgical site complications; surgical site infection; deep surgical site infection
Starting date	2017
Contact information	eric.synatschk@acelity.com; jane.hart@kci1.com
Notes	

NCT03321799

Trial name or title	Comparison of negative pressure wound therapy versus conventional dressings for the prevention of wound complications after revision THA
Methods	Randomised controlled trial
Participants	Patients > 18 years of age undergoing a revision total hip arthroplasty procedure
Interventions	Negative pressure wound therapy versus sterile antimicrobial dressings
Outcomes	Wound complications; reoperation; cost comparison
Starting date	2017
Contact information	chris.culvern@rushortho.com
Notes	

NCT03345771

Trial name or title	Antimicrobial barrier dressing versus closed-incision negative pressure therapy in the obese primary total joint arthroplasty
Methods	Randomised controlled trial
Participants	Patients identified at preoperative testing to have an elevated BMI (> 35)

NCT03345771 *(Continued)*

Interventions	Negative pressure wound therapy versus antimicrobial barrier dressing
Outcomes	Visual analogue scale pain score; wound evaluation scale
Starting date	2017
Contact information	Afshin.Anoushiravani@nyumc.org
Notes	

NCT03346694

Trial name or title	Reducing surgical site infection rates using an alternative sternal dressing
Methods	Randomised controlled trial
Participants	Patients who will undergo cardiac surgery via a sternotomy incision
Interventions	Standard island dressing versus PREVENA negative pressure versus Mepilex Border Post-Op Ag
Outcomes	Rates of surgical site infection pertaining to each dressing studied; impact of alternative dressings on rates of sternal wound incision infection
Starting date	2017
Contact information	jackboyd@stanford.edu; jniesen@stanfordhealthcare.org
Notes	

NCT03395613

Trial name or title	Negative pressure incision management system in infrainguinal vascular surgery
Methods	Randomised controlled trial
Participants	Not stated
Interventions	Negative pressure wound therapy versus standard sterile gauze dressing
Outcomes	Postoperative SSI; postoperative SSI within 90 days; antibiotic prescriptions for skin and soft tissue infections; postoperative SSI within 90 days requiring surgical revision; adverse events directly related the NPWT dressing; major lower limb amputation and/or mortality; changes in reported quality of life; assessment of healthcare-related costs; assessment of quality of life during the first 7-day period
Starting date	2018
Contact information	alireza.daryapeyma@sll.se; rebecka.hultgren@sll.se
Notes	

NCT03402945

Trial name or title	Prevention of infections in cardiac surgery (PICS) Prevena study (PICS-Prevena)
Methods	Randomised controlled trial - 4-arm factorial design
Participants	Patients ≥ 18 years of age undergoing open-heart surgery
Interventions	PREVENA and cefazolin versus PREVENA and cefazolin and vancomycin versus standard wound dressing and cefazolin versus standard wound dressing and cefazolin and vancomycin
Outcomes	Adherence to the wound management system; adherence to the antibiotic regimen; loss of follow-up; deep incisional and organ/space sternal surgical site infection; wound dehiscence; *Clostridium difficile* infection; mortality in participants with an active infection; intensive care unit and hospital stay; pain on day 7; acute kidney injury
Starting date	2018
Contact information	prevena@phri.ca
Notes	

NCT03414762

Trial name or title	PICO negative pressure wound therapy in obese women undergoing elective cesarean delivery
Methods	Randomised controlled trial
Participants	Obese women undergoing elective caesarean delivery
Interventions	Negative pressure wound therapy versus standard wound dressings
Outcomes	Surgical site occurrence; surgical incision intervention
Starting date	November 2018
Contact information	Sarah Pachtman (spachtman@northwell.edu)
Notes	

NCT03433937

Trial name or title	Prevention of seroma following inguinal lymph node dissection with prophylactic incisional negative pressure wound therapy
Methods	Randomised controlled trial
Participants	Malignant melanoma patients who are candidates for inguinal lymph node dissection and are 18 years of age or older
Interventions	Negative pressure wound therapy versus Micropore tape
Outcomes	Number of participants with seroma; number and volume of seromas per participant; number of participants with: surgical wound infection; wound rupture; wound necrosis; haematoma; lym-

NCT03433937 *(Continued)*

	phoedema; regional recurrence; reoperations; questionnaire EQ-5D-5L; hospitalisation time; hospitalisation readmission time; LYMQOL questionnaire
Starting date	2018
Contact information	Mads.Gustaf.Jorgensen@rsyd.dk
Notes	

NCT03458663

Trial name or title	Randomized trial comparing Prevena and ActiV.A.C. system to conventional care after Bascom's cleft lift surgery
Methods	Randomised controlled trial
Participants	Patients with recurrence after previous surgery for pilonidal disease, cases of poor postoperative healing, or primary extensive/fistulating disease referred to Randers Regional Hospital for assessment for reconstructive Bascom's cleft lift surgery
Interventions	PREVENA versus conventional postoperative care
Outcomes	Primary healing; health perception; long-term healing; early recurrence; postoperative pain
Starting date	2018
Contact information	susahaas@rm.dk; marlesoe@rm.dk
Notes	

NCT03460262

Trial name or title	Negative pressure wound therapy for prevention of groin infection following vascular surgery (PICO)
Methods	Randomised controlled trial
Participants	High-risk patients undergoing vascular surgery with groin incision (without ongoing infection)
Interventions	PICO versus standard cutiplast
Outcomes	Rate of wound complications
Starting date	2018
Contact information	parla.astarci@uclouvain.be; julien.possoz@uclouvain.be
Notes	

NCT03512470

Trial name or title	Clinical study on the prevention of surgical wound complications for aneurysmal thoracic-abdominal aortic pathology using the "PREVENA" system (TVAC)
Methods	Randomised controlled trial
Participants	Patients with surgical wounds to treat thoracic-abdominal aortic pathology
Interventions	PREVENA versus standard medication
Outcomes	Reduction of surgical site infections; reduction of adverse events
Starting date	2018
Contact information	domenico.baccellieri@hsr.it; elisa.simonini@hsr.it
Notes	

Nguyen 2017

Trial name or title	Nguyen 2017
Methods	Single-institution, prospective, randomised, open-label, superiority trial
Participants	Patients scheduled for elective colorectal resection with or without creation of an ostomy (open or laparoscopic)
Interventions	Patients will be randomised to receive NPWT or conventional dressings.
Outcomes	Primary outcomes will be wound complications within the first 30 postoperative days. SSI rate will also be reported as a subgroup analysis. Secondary outcomes will include length of stay, number of postoperative visits in the 30-day period, complications, wound VAC-specific complications, and patient satisfaction.
Starting date	Unclear
Contact information	University of British Columbia (no contact details available)
Notes	Very limited information available.

NL6488

Trial name or title	PREventing Surgical Site occurrences using negative pressURE wound therapy?
Methods	Randomised controlled trial
Participants	Patients scheduled for elective, open abdominal wall reconstruction
Interventions	Negative pressure wound therapy versus conventional wound care
Outcomes	Surgical site occurrence; QoL; recurrence 1 year after surgery; individual components of primary outcome SSO; peri-incisional SSO; percentage of participants with signs of SSO on photographs by blinded outcome assessment; frequency and type of procedures related to SSO; hospital stay after

NL6488 *(Continued)*

	surgery in days; earlier removal of iNPWT because of SSO; emergency department visits after discharge; readmission; non-primary outcome complications; cost-effectiveness
Starting date	2017
Contact information	p.r.zwanenburg@amc.nl
Notes	Previously registered as NTR6675; starting date may not reflect previous registration

NTR5808

Trial name or title	Dehiscence prevention study
Methods	Randomised controlled trial
Participants	Patients undergoing 1 of the following elective surgeries: plastic surgery through a transverse abdominal or subgluteal incision
Interventions	PREVENA incision management system versus simple cotton wound dressing
Outcomes	Wound dehiscence; surgical site infection; pain; allergy to the wound dressing
Starting date	2015
Contact information	Emmy.Muller-Sloof@Radboudumc.nl
Notes	

NTR6481

Trial name or title	Randomized controlled clinical trial incisional NPWT versus sterile surgical dressing for surgical wounds after arterial vascular surgery
Methods	Randomised controlled trial
Participants	Patients undergoing bypass: aortic-iliacal, iliacal-femoral, femoral-femoral, femoral-popliteal, femoral-crural, femoral-tibial; endarterectomy: iliacal, femoral; reconstruction aneurysm: femoral; embolectomy: iliacal, femoral
Interventions	Incisional negative pressure wound therapy versus sterile surgical dressing
Outcomes	Incidence of wound complications; complete wound-healing percentages; hospital stay in days; additional surgery; readmissions; extra visits to the outpatient clinic
Starting date	2017
Contact information	prevenastudie@haaglandenmc.nl
Notes	

SUNRRISE 2017	
Trial name or title	SUNRRISE: Single Use Negative pRessure dressing for Reduction In Surgical site infection following Emergency laparotomy
Methods	Randomised controlled trial
Participants	Patients undergoing emergency laparotomy
Interventions	Portable single-use NPWT dressings Standard dressings
Outcomes	SSI at 30 days; length of stay; readmission; re-intervention; adverse events; pain; HRQoL; cost-effectiveness
Starting date	November 2017
Contact information	Dr Laura Magill, University of Birmingham, UK
Notes	ISRCTN17599457

AE: adverse event
BMI: body mass index
CABG: coronary artery bypass graft
CRS: cryoreduction surgery
CS: caesarean section
HPBS: hepatopancreatobiliary surgery
HRQoL: health-related quality of life
iNPWT: incisional negative pressure wound therapy
LDex: lymphedema index
LYMQOL: Lymphoedema Quality-of-Life Questionnaire
MRSA: methicillin-resistant Staphylococcus aureus
NPWT: negative pressure wound therapy
QoL: quality of life
RCT: randomised controlled trial
SAE: serious adverse event
SSI: surgical site infection
SSO: surgical site occurrence
THA: total hip arthroplasty
TKA: total knee arthroplasty
VAC: vacuum-assisted closure

DATA AND ANALYSES

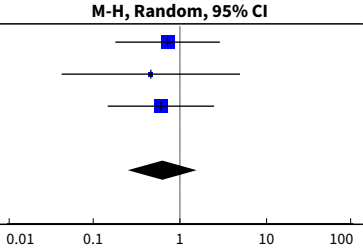
Comparison 1. Negative pressure wound therapy versus standard dressing

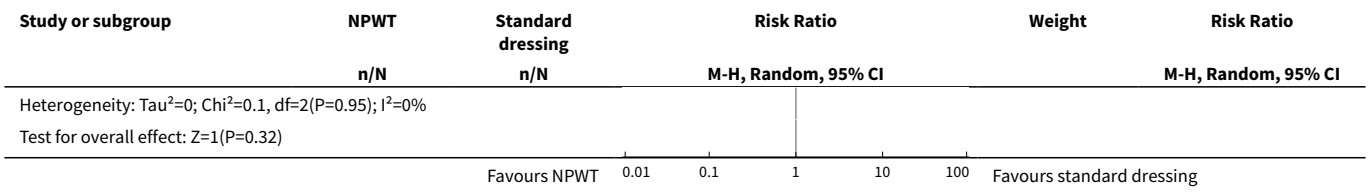
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality	3	416	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.25, 1.56]
2 Surgical site infection	23	2547	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.53, 0.85]
2.1 Abdominal and colorectal surgery	5	520	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.35, 1.37]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.2 Caesarean	5	849	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.54, 1.21]
2.3 Hip/knee arthroplasties	3	339	Risk Ratio (M-H, Random, 95% CI)	0.56 [0.19, 1.64]
2.4 Groin	4	416	Risk Ratio (M-H, Random, 95% CI)	0.48 [0.30, 0.74]
2.5 Fractures	2	157	Risk Ratio (M-H, Random, 95% CI)	2.32 [0.76, 7.07]
2.6 Vascular surgery	1	56	Risk Ratio (M-H, Random, 95% CI)	0.27 [0.01, 6.37]
2.7 Sternotomy surgery	1	80	Risk Ratio (M-H, Random, 95% CI)	0.14 [0.02, 1.11]
2.8 Laparotomy	1	49	Risk Ratio (M-H, Random, 95% CI)	0.26 [0.06, 1.10]
2.9 Mixed	1	81	Risk Ratio (M-H, Random, 95% CI)	0.50 [0.13, 1.97]
3 Dehiscence	12	1507	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.55, 1.18]
4 Reoperation	6	1021	Risk Ratio (M-H, Random, 95% CI)	1.09 [0.73, 1.63]
5 Readmission	7	1271	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.47, 1.57]
6 Seroma - incidence	6	568	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.45, 1.00]
7 Seroma - mean volume	2	39	Mean Difference (IV, Random, 95% CI)	-1.70 [-3.32, -0.08]
8 Seroma - mean size	1	21	Mean Difference (IV, Random, 95% CI)	-3.74 [-6.88, -0.60]
9 Haematoma	6	831	Risk Ratio (M-H, Random, 95% CI)	1.05 [0.32, 3.42]
10 Skin blisters	6	597	Risk Ratio (M-H, Random, 95% CI)	6.64 [3.16, 13.95]
11 Dressing cost	2		Mean Difference (IV, Random, 95% CI)	Totals not selected
12 Resource use	2	296	Mean Difference (IV, Random, 95% CI)	63.04 [-31.50, 157.59]
13 QALY	2	296	Mean Difference (IV, Random, 95% CI)	0.00 [-0.00, 0.00]

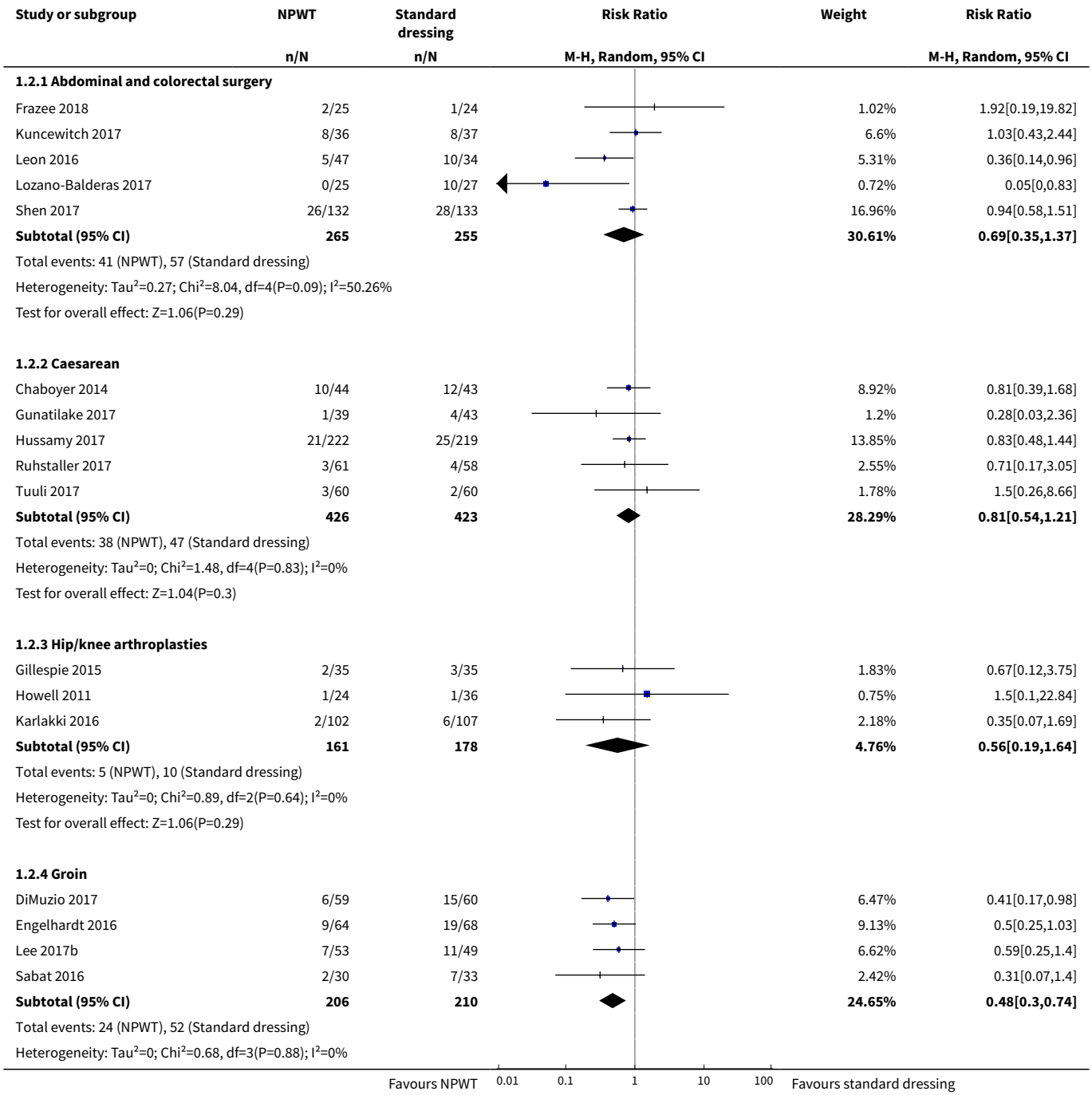
Analysis 1.1. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 1 Mortality.

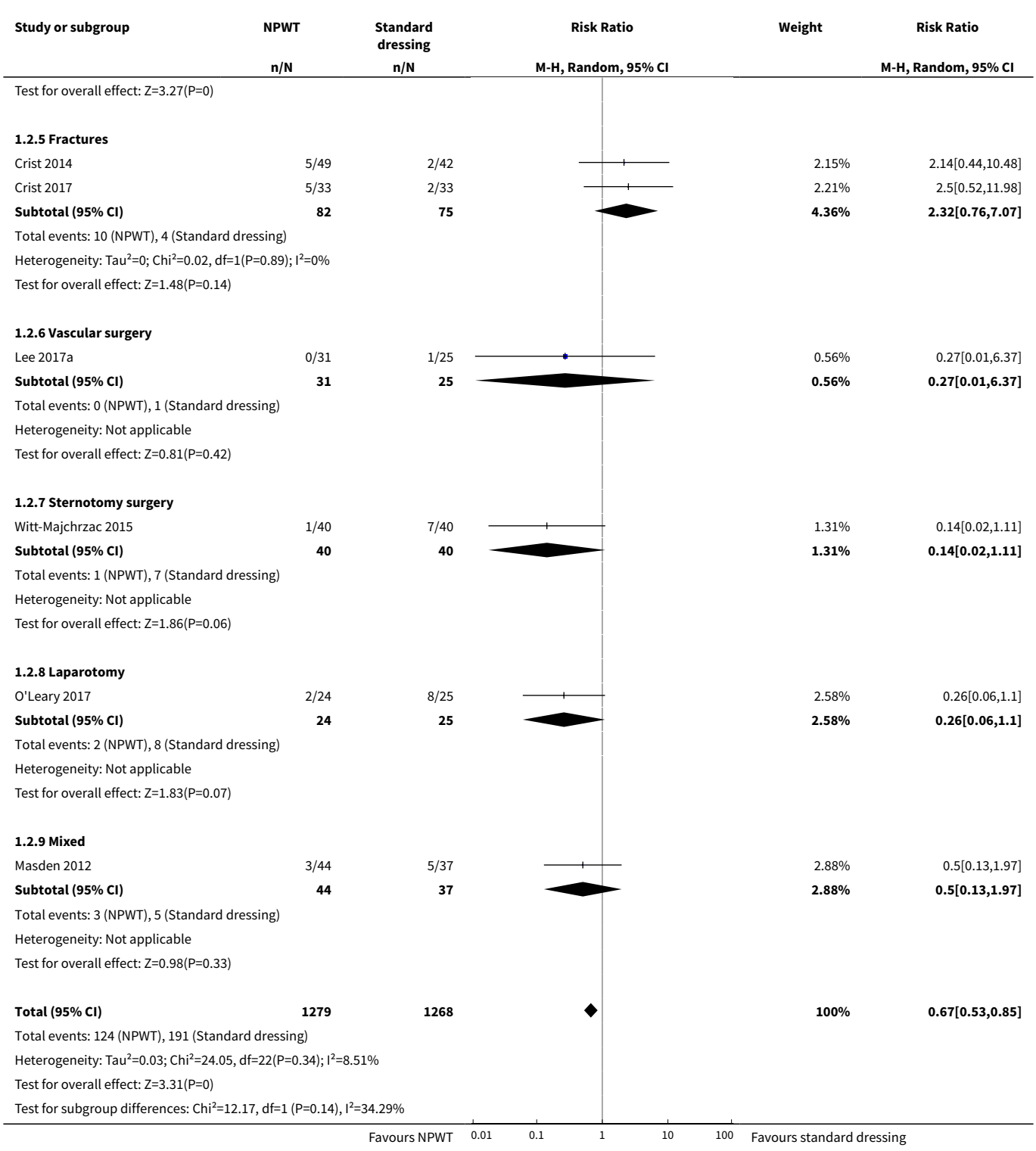
Study or subgroup	NPWT	Standard dressing	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H, Random, 95% CI		M-H, Random, 95% CI
Frazee 2018	3/25	4/24		43.26%	0.72[0.18,2.89]
Lee 2017b	1/53	2/49		14.86%	0.46[0.04,4.94]
Shen 2017	3/132	5/133		41.88%	0.6[0.15,2.48]
Total (95% CI)	**210**	**206**		**100%**	**0.63[0.25,1.56]**
Total events: 7 (NPWT), 11 (Standard dressing)					





Analysis 1.2. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 2 Surgical site infection.





Analysis 1.3. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 3 Dehiscence.

Study or subgroup	NPWT n/N	Standard dressing n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
DiMuzio 2017	5/59	11/60		14.94%	0.46[0.17,1.25]
Frazee 2018	1/25	0/24		1.49%	2.88[0.12,67.53]
Gillespie 2015	1/35	1/35		1.98%	1[0.07,15.36]
Gunatilake 2017	1/39	5/43		3.34%	0.22[0.03,1.81]
Hussamy 2017	4/222	1/219		3.1%	3.95[0.44,35.02]
Kuncewitch 2017	1/36	2/37		2.66%	0.51[0.05,5.42]
Masden 2012	16/44	11/37		37.08%	1.22[0.65,2.3]
Sabat 2016	3/30	8/33		9.74%	0.41[0.12,1.41]
Shen 2017	3/132	3/133		5.9%	1.01[0.21,4.9]
Tanaydin 2018	5/32	10/32		16.18%	0.5[0.19,1.3]
Tuuli 2017	2/60	0/60		1.62%	5[0.25,102]
Witt-Majchrzac 2015	1/40	1/40		1.97%	1[0.06,15.44]
Total (95% CI)	**754**	**753**		**100%**	**0.8[0.55,1.18]**
Total events: 43 (NPWT), 53 (Standard dressing)					
Heterogeneity: Tau^2=0; Chi^2=10.77, df=11(P=0.46); I^2=0%					
Test for overall effect: Z=1.13(P=0.26)					

Favours NPWT — Favours standard dressing

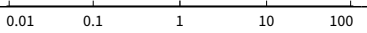
Analysis 1.4. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 4 Reoperation.

Study or subgroup	NPWT n/N	Standard dressing n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Gunatilake 2017	1/39	6/43		3.81%	0.18[0.02,1.46]
Hussamy 2017	14/222	10/219		26.22%	1.38[0.63,3.04]
Lee 2017b	2/53	1/49		2.91%	1.85[0.17,19.76]
Masden 2012	9/44	8/37		22.85%	0.95[0.41,2.2]
O'Leary 2017	0/25	1/25		1.64%	0.33[0.01,7.81]
Shen 2017	19/132	16/133		42.56%	1.2[0.64,2.22]
Total (95% CI)	**515**	**506**		**100%**	**1.09[0.73,1.63]**
Total events: 45 (NPWT), 42 (Standard dressing)					
Heterogeneity: Tau^2=0; Chi^2=4.15, df=5(P=0.53); I^2=0%					
Test for overall effect: Z=0.41(P=0.69)					

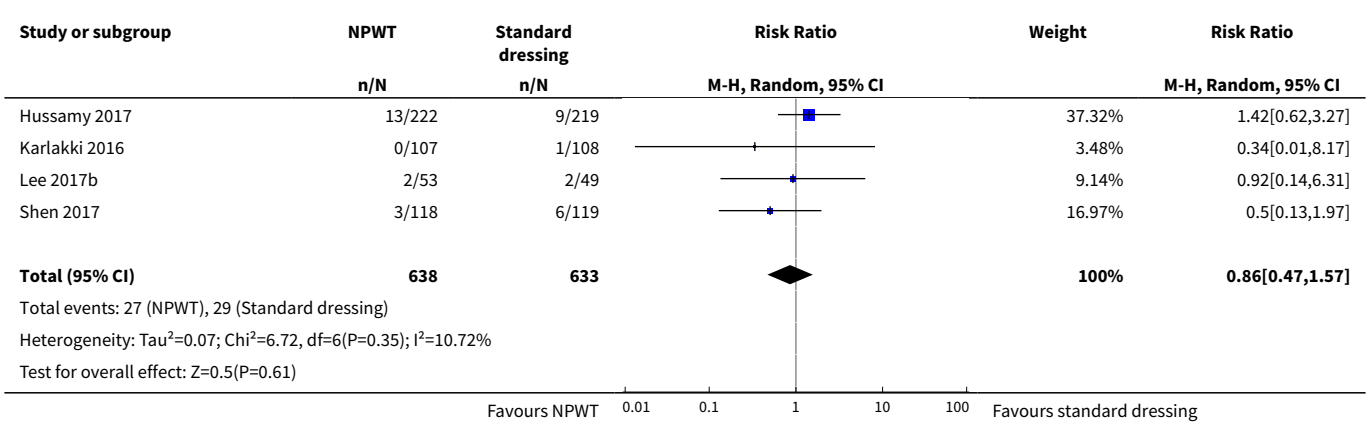
Favours NPWT — Favours standard dressing

Analysis 1.5. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 5 Readmission.

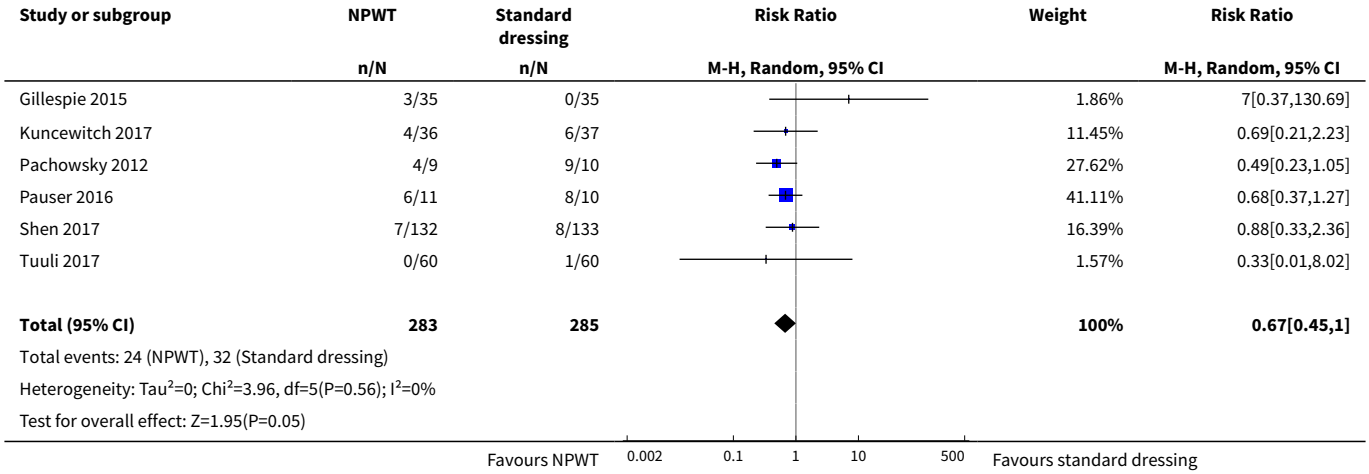
Study or subgroup	NPWT n/N	Standard dressing n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Chaboyer 2014	1/44	1/43		4.67%	0.98[0.06,15.13]
DiMuzio 2017	4/59	10/60		24.2%	0.41[0.14,1.23]
Gillespie 2015	4/35	0/35		4.22%	9[0.5,161.13]



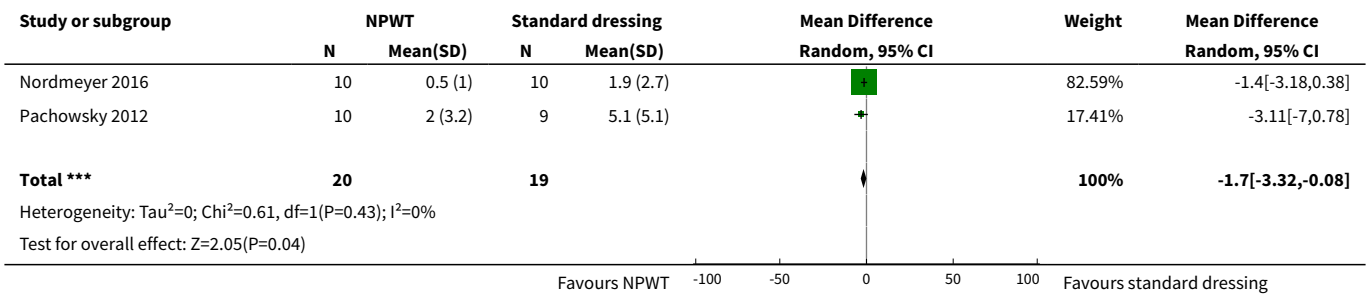
Favours NPWT — Favours standard dressing



Analysis 1.6. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 6 Seroma - incidence.

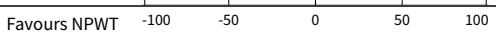


Analysis 1.7. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 7 Seroma - mean volume.



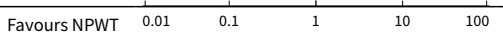
Analysis 1.8. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 8 Seroma - mean size.

Study or subgroup	NPWT N	NPWT Mean(SD)	Standard dressing N	Standard dressing Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Pauser 2016	11	0.3 (0.8)	10	4 (5)		100%	-3.74[-6.88,-0.6]
Total ***	**11**		**10**			**100%**	**-3.74[-6.88,-0.6]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2.34(P=0.02)							



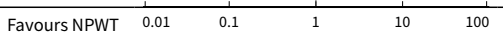
Analysis 1.9. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 9 Haematoma.

Study or subgroup	NPWT n/N	Standard dressing n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Chaboyer 2014	1/44	4/43		30.19%	0.24[0.03,2.1]
Gillespie 2015	3/35	1/35		28.48%	3[0.33,27.46]
Karlakki 2016	0/102	1/107		13.73%	0.35[0.01,8.48]
Shen 2017	1/132	0/133		13.71%	3.02[0.12,73.53]
Tuuli 2017	0/60	0/60			Not estimable
Witt-Majchrzac 2015	1/40	0/40		13.89%	3[0.13,71.51]
Total (95% CI)	**413**	**418**		**100%**	**1.05[0.32,3.42]**
Total events: 6 (NPWT), 6 (Standard dressing)					
Heterogeneity: Tau^2=0; Chi^2=3.94, df=4(P=0.41); I^2=0%					
Test for overall effect: Z=0.08(P=0.94)					



Analysis 1.10. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 10 Skin blisters.

Study or subgroup	NPWT n/N	Standard dressing n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Chaboyer 2014	4/44	0/43		6.59%	8.8[0.49,158.66]
Howell 2011	15/24	3/36		43.43%	7.5[2.43,23.14]
Karlakki 2016	11/102	1/107		13.4%	11.54[1.52,87.78]
Manoharan 2016	1/21	0/21		5.57%	3[0.13,69.7]
Ruhstaller 2017	8/61	2/58		24.28%	3.8[0.84,17.17]
Witt-Majchrzac 2015	5/40	0/40		6.73%	11[0.63,192.56]
Total (95% CI)	**292**	**305**		**100%**	**6.64[3.16,13.95]**
Total events: 44 (NPWT), 6 (Standard dressing)					
Heterogeneity: Tau^2=0; Chi^2=1.28, df=5(P=0.94); I^2=0%					
Test for overall effect: Z=5(P<0.0001)					



Analysis 1.11. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 11 Dressing cost.

Study or subgroup	NPWT		Standard dressing		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Gillespie 2015	35	38.4 (13.6)	35	3 (1.2)		35.39[30.87,39.91]
Manoharan 2016	21	258.9 (28.5)	21	43.5 (64.2)		215.43[185.37,245.49]

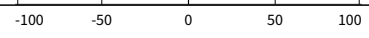
Analysis 1.12. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 12 Resource use.

Study or subgroup	NPWT		Standard dressing		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Heard 2017	44	2871.5 (182.1)	43	2806.6 (260.4)		99.84%	64.9[-29.72,159.52]
Nherera 2017	102	5602 (7954)	107	6713 (9559)		0.16%	-1111[-3490.74,1268.74]
Total ***	**146**		**150**			**100%**	**63.04[-31.5,157.59]**
Heterogeneity: Tau^2=0; Chi^2=0.94, df=1(P=0.33); I^2=0%							
Test for overall effect: Z=1.31(P=0.19)							

Favours NPWT Favours Standard dressing

Analysis 1.13. Comparison 1 Negative pressure wound therapy versus standard dressing, Outcome 13 QALY.

Study or subgroup	NPWT		Standard dressing		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Heard 2017	44	0.1 (0)	43	0.1 (0)		29.4%	0[-0,0.01]
Nherera 2017	102	0.1 (0)	107	0.1 (0)		70.6%	0[-0,0]
Total ***	**146**		**150**			**100%**	**0[-0,0]**
Heterogeneity: Tau^2=0; Chi^2=0, df=1(P=1); I^2=0%							
Test for overall effect: Z=0.86(P=0.39)							



Favours NPWT Favours standard dressing

ADDITIONAL TABLES

Table 1. Study details

Study	Wounds characteristics	Comparison	Time points	Mortality	SSI	Dehiscence	Re-operation	Readmission	Seroma incidence	Seroma – mean volume	Haematoma – mean size	Skin blisters	Pain	QoL	Length of stay	Resource used costs	QALYs	Notes
Chaboyer 2014	Caesarean section in obese women	Group A: PICO dressing Group B: Comfeel dressing	1, 2, 3, and 4 weeks post-surgery	-	Group A: 10/44 Group B: 12/43	-	-	Group A: 1/44 Group B: 1/43	-	-	Group A: 1/44 Group B: 4/43	Group A: 4/44 Group B: 0/43	-	-	-	-	-	-
Crist 2014	Open reduction and internal fixation of hip, pelvis, and acetabular fracture surgery	Group A: NPWT Group B: standard gauze dressing	12 months	-	Group A: 5/49 Group B: 2/42	-	-	-	-	-	-	-	-	-	-	-	-	-
Crist 2017	Open reduction internal fixation (ORIF) for acetabular fractures	Group A: NPWT Group B: standard gauze dressing	10 to 21 days, 6 weeks, 12 weeks, and every 6 to 8 weeks thereafter until bony union occurred	-	Group A: 5/33 Group B: 2/33 *completed-case analysis - 5 lost after randomisation but group allocation not known*	-	-	-	-	-	-	-	-	-	-	-	-	Infection defined as "deep infection"
DiMuzio 2017 Abstract	Groin wounds	Group A (59, high risk): NPWT dressing Group B (60, high risk): standard gauze dressing Group C (21, low risk): standard gauze dressing	30 days	-	Group A: 6/59 Group B: 15/60 Group C: 1/21	Group A: 8.5% Group B: 18.3% Group C: 4.8%	-	Group A: 6.8% Group B: 16.7% Group C: 4.8%	-	-	-	-	-	-	Group A: USD 30,492 Group B: USD 36,537 Group C:	-	Contacted authors for full text Group C not included in data analysis due to baseline heterogeneity.

Table 1. Study details *(Continued)*

																	USD 17,599 NPWT reduced cost per patient of USD 6045 (USD 30,492 + USD 500 (device) in NWPT group vs USD 36,537 in dressing group). Unsuitable for further analysis		
Engelhardt 2016	Groin wound	Group A: NPWT Group B: conventional dressing	5 and 42 days	-	Group A: 9/64 Group B: 19/68	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Table 1. Study details *(Continued)*

Frazee 2018	Celiotomy with either class III or class IV surgical wounds	Group A (25): closed-NPWT Group B (24): open-NPWT	Not reported	Group A: 3/25 Group B: 4/24 *died from complications unrelated to the wound*	Group A: 2/25 Group B: 1/24	Group A: 1/25 Group B: 0/24	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Gillespie 2015	Primary hip arthroplasty	Group A: PICO dressing Group B: Comfeel dressing	30 days and 6 weeks post-surgery	-	Group A: 2/35 Group B: 3/35	Group A: 1/35 Group B: 1/35	-	Group A: 4/35 Group B: 0/35	Group A: 3/35 Group B: 0/35	-	Group A: 3/35 Group B: 1/35	-	-	Group A: AUS 38.4 ± AUS 13.6 Group B: AUS 3.01 ± AUS 1.2	-	QoL reported in Heard 2017.				
Gunatilake 2017	Caesarean	Group A: NPWT Group B: standard care dressing	42 ± 10 days postoperatively (days 1, 2, 6, 14, and 42)	-	Group A: 1/39 Group B: 4/43	Group A: 1/39 Group B: 5/43	Group A: 1/39 Group B: 6/43	-	-	-	-	-	Pain reductions at rest	-	-	-	-	ITT: n = 92; 82 completed the study		

Table 1. Study details *(Continued)*

																Group A: 39/46 Group B: 20/46 Pain reductions with incisional pressure Group A: 42/46 Group B: 25/46			
Heard 2017	Caesarean section in obese women	Group A: NPWT Group B: standard care	4 weeks postdischarge	-		-		-	-	-	-	-	-	-	-	Group A (44): 2871.5 ± 182.1 AUD Group B (43): 2806.6 ± 260.4 AUD	Group A (44): 0.067 ± 0.01 Group B (43): 0.066 ± 0.01	Data drawn from Chaboyer 2014.
Howell 2011	Knee arthroplasty	Group A: NPWT Group B: gauze dressing	Followed up for 12 months postsurgery	-	Group A: 1/24 Group B: 1/36	-		-	-	-	-	-	-	Group A: 15/24		-	-	-	

Table 1. Study details *(Continued)*

																	Group B: 3/36		
Hussamy 2017 Abstract	Caesarean	Group A (222): NPWT Group B (219): standard dressing	30 days post-delivery	-	*Superficial SSI* Group A: 20/222 Group B: 25/219 *Organ SSI* Group A: 1/222 Group B: 0/219	Group A: 4/222 Group B: 1/219	-	Group A: 14/222 Group B: 10/219	-	-	-	-	-	-	-	-	Unable to contact authors
Karlakki 2016	Total hip or knee arthroplasties	Group A: PICO dressing Group B: Comfeel dressing	1, 2, and 6 weeks post-surgery	-	Group A: 2/102 Group B: 6/107	-	-	Group A: 0/107 Group B: 1/108	-	-	Group A: 0/102 Group B: 1/107	Group A: 11/102 Group B: 1/107	-	-	-	-	-
Kuncewitch 2017 Abstract	Pancreatectomy	Group A (36): NPWT Group B (37): standard surgical dressing	30 days post-surgery follow-up	-	*Superficial SSI* Group A: 5/36 Group B: 6/37 *Deep SSI* Group A: 3/36 Group B: 2/37	Group A: 1/36 Group B: 2/37	-	-	Group A: 4/36 Group B: 6/37	-	-	-	-	-	-	-	Unable to contact authors
Lee 2017a	Great saphenous vein harvest	Group A (33): NPWT Group B (27): standard surgical dressing	Initial assessment: not specified; endpoint assessment: 6 weeks	-	Group A: 0/31 Group B: 1/25	-	-	-	-	-	-	-	-	-	EQ-5D-3L: Group A (n = 26): 78	-	2 participants died (sepsis; stroke). 2 participants were delirious and unable to com-

Table 1. Study details *(Continued)*

														Group B (n = 17): 63 *P* = *0.172*			plete QoL, all other objective evaluations were done (all 4 in NPWT).
Lee 2017b	High-risk groin wounds	Group A (53): NPWT Group B (49): standard care	30 days and 90 days	Mortality within 90 days Group A: 1/53 Group B: 2/49	*In-hospital SSI* Group A: 1/53 Group B: 1/49 *30-day SSI* Group A: 6/53 Group B: 9/49 *90-day SSI* Group A: 7/53 Group B: 11/49	-	Group A: 2/53 Group B: 1/49 *for SSI*	Group A: 2/53 Group B: 2/49 *for SSI*	-	-	-	-	-	-	-	-	-	Latest time point of SSI data used for analysis.
Leon 2016 Abstract	Open colorectal surgery	Group A (47): NPWT Group B (34): usual dressing	15-day and 30-day evaluation	-	Group A: 5/47 Group B: 10/34	-	-	-	-	-	-	-	-	-	-	-	-	Unable to contact authors
Lozano-Balderas 2017	Laparotomised patients with class III or IV (contaminated/dirty-infected) surgical wounds	Group A (25): vacuum-assisted closure Group B (27): primary closure Group C (29): delayed primary closure	Daily when in hospital or in a 30-day period after surgery	-	Group A: 0/25 Group B: 10/27 Group C: 5/29	-	-	-	-	-	-	-	-	-	-	-	-	Group C (delayed primary closure) not included in data analysis due to irrelevant wounds.
Manoharan 2016	Primary arthroplasty	Group A: NPWT Group B: conventional dry dressing	10 to 12 days postsurgery	-	-	-	-	-	-	-	-	-	Group A: 1/21	-	Group A: AUS 285.94	-	-	

Table 1. Study details *(Continued)*

											Group B: 0/21	± AUS 28.54 Group B: AUS 43.51 ± AUS 64.23			
Masden 2012	Radial forearm free flap	Group A: NPWT Group B: dry dressing	Not clear	-	Group A: 3/44 Group B: 5/37	Group A: 16/44 Group B: 11/37	Group A: 9/44 Group B: 8/37	-	-	- -	- -	- -	-	-	-
Nhera 2017	Primary hip and knee replacements	Group A: PICO dressing Group B: Comfeel dressing	6 weeks follow-up	-	-	-	-	-	-	- -	- -	- -	Group A (102): 5602 ± 7954 GBP Group B (107): 6713 ± 9559 GPB	Group A (102): 0.116 ± 0.01 Group B (107): 0.115 ± 0.01	Data drawn from Karlakki 2016.
Nordmeyer 2016	Spinal fractures treated with internal fixation	Group A: PICO dressing Group B: standard dressing	Day 5 and day 10 after surgery	-	-	-	-	-	-	-	Group A (10): 0.5 ± 1 Group B (10):	- -	- -	-	- -

Table 1. Study details *(Continued)*

										1.9 ± 2.7									
O'Leary 2017	Open abdominal surgery	Group A: PICO dressing Group B: transparent waterproof dressing	Day 4 and day 30 post-surgery	-	Group A: 2/24 Group B: 8/25	-	Group A: 0/25 Group B: 1/25	-	-	-	-	-	Reported "no difference"	-	-	-	-	-
Pachowsky 2012	Hip arthroplasty	Group A: NPWT Group B: standard dressing	Day 5 and day 10 in postoperative period	-	-	-	-	-	Group A: 4/9 Group B: 9/10	Group A (10): 1.97 ± 3.21 Group B (9): 5.08 ± 5.11	-	-	-	-	-	-	-	Very small sample size
Pauser 2016	Fractures of the femoral neck treated by hemiarthroplasty	Group A: NPWT Group B: standard dressing	Day 5 and day 10 after surgery	-	-	-	-	-	Group A: 6/11 Group B: 8/10	Group A (11): 0.26 ± 0.75 Group B (10): 4 ± 5.01	-	-	-	-	-	-	-	Very small sample size
Pleger 2018	Groin wound	Group A: NPWT (n = 58 incisions)	Days 5 to 7 and 30 after surgery	-	Group A: 1/58 Group B: 10/71	*Superficial wound*	-	-	Group A: 0/58	-	Group A: 0/58	-	-	-	-	-	-	Unit of analysis error: 100 participants

Table 1. Study details *(Continued)*

		Group B: control dressing (n = 71 incisions)				*dehiscence* Group A: 3/58 Group B: 4/71 *Deep wound dehiscence with fat necrosis* Group A: 1/58 Group B: 4/71			Group B: 1/71		Group B: 8/71					with 129 groin incisions	
Ruhstaller 2017	Unplanned caesarean section	Group A: NPWT Group B: standard care	4 weeks postsurgery	-	Group A: 3/61 Group B: 4/58	-	-	-	-	-	-	-	Group A: 8/61 Group B: 2/58	Reported "no difference"	-	-	-	-	-
Sabat 2016 Abstract	Groin wounds in vascular surgery	Group A: NPWT Group B: conventional dressing (gauze and Tegaderm)	4 months postsurgery	-	Group A: 2/30 Group B: 7/33	Group A: 3/30 Group B: 8/33	-	-	-	-	-	-	-	-	-	-	-	-
Shen 2017	Open resection of intra-abdominal neoplasms	Group A: PICO dressing Group B: Comfeel dressing	30 days after surgery	Group A: 3/132 Group B: 5/133	Group A: 26/132 Group B: 28/133	Group A: 3/132 Group B: 3/133	Group A: 19/132 Group B: 16/133	Group A: 32/132 Group B: 53/133	Group A: 7/132 Group B: 8/133	-	Group A: 1/132 Group B: 0/133	-	-	-	-	-	-	-

Table 1. Study details *(Continued)*

Stannard 2012	Tibial plateau, pilon, or calcaneus fracture	Group A: NPWT Group B: standard dressing	Not stated	-	Group A: 14/144 Group B: 23/122	Group A: 12/139 Group B: 20/122	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Unit of analysis error
Tanaydin 2018	Bilateral breast reduction mammoplasty	Group A: NPWT Group B: standard care (fixation strips)	21 days	-	-	Group A: 5/32 Group B: 10/32	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	32 participants served as their own control.
Tuuli 2017	Caesarean delivery	Group A: NPWT Group B: standard dressing	30 days	-	Group A: 3/60 Group B: 2/60	Group A: 2/60 Group B: 0/60	-	-	Group A: 0/60 Group B: 1/60	-	Group A: 0/60 Group B: 0/60	Pain score (on 0-to-10 scale) was significantly lower with prophylactic NPWT (median (IQR): 0 (0, 1) vs 1 (0, 3),	-	-	-	-	-					

Table 1. Study details *(Continued)*

														P = 0.02).					
Witt-Majchrzac 2015	Coronary artery bypass surgery	Group A: NPWT Group B: conventional dressing	6 weeks follow-up	-	Group A: 1/40 Group B: 7/40	Group A: 1/40 Group B: 1/40	-	-	-	-	-	Group A: 1/40 Group B: 1/40	Group A: 5/40 Group B: 0/40	-	-	-	-	-	-

ICER: incremental cost-effectiveness ratio
IQR: interquartile range
ITT: intention-to-treat
NPWT: negative pressure wound therapy
QALY: quality-adjusted life year
QoL: quality of life
SSI: surgical site infection

Table 2. Quality assessment of economic studies using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist

Sections	Items	Item Number	Heard (2017)	Nherera (2017)
Title and abstract	Title	1	✓	✓
	Abstract	2	✓	✓
Introduction	Background and objectives	3	✓	✓
Methods	Target population and subgroups	4	✓	✓
	Setting and locations	5	✓	✓
	Study perspectives	6	✓	✓
	Comparators	7	✓	✓
	Time horizon	8	X	✓
	Discount rate	9	✓	✓
	Choice of health outcomes	10	✓	≠
	Measurement of effectiveness	11a	≠	N/A
		11b	N/A	✓
	Measurement and valuation of preference-based outcomes	12	≠	≠
	Estimating resources and costs	13a	✓	N/A
		13b	N/A	✓
	Currency, price date, and conversion	14	✓	≠
	Choice of model	15	≠	≠
	Assumptions	16	✓	✓
	Analytical methods	17	✓	✓
Results	Study parameters	18	✓	✓
	Incremental costs and outcomes	19	✓	✓
	Characterising uncertainty	20a	≠	N/A
		20b	N/A	≠
	Characterising heterogeneity	21	X	✓
Discussion	Study findings, limitations, generalisability, and current knowledge	22	✓	✓

Table 2. Quality assessment of economic studies using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist *(Continued)*

Others	Source of funding	23	✓	X
	Conflicts of interest	24	✓	✓
Total			20/24 (83.3%)	20.5/24 (85.4%)

✓ Item met in full; ≠ Item partially met; X Item not met; N/A = Not applicable
Full explanation of CHEERS items (Husereau 2013) available at: http://www.ispor.org/workpaper/CHEERS/revised-CHEERS-Checklist-Oct13.pdf

APPENDICES

Appendix 1. Glossary of terms

Term	Description
Dehiscence	Wound dehiscence is a complication of surgery in which a wound breaks open along the line of the surgical incision.
Negative pressure wound therapy (NPWT)	Negative pressure wound therapy is based on a closed, sealed system that produces negative pressure to the wound surface. The wound is covered or packed with an open-cell foam or gauze dressing and sealed with an occlusive drape. Intermittent or continuous suction is maintained by connecting suction tubes from the wound dressing to a vacuum pump and liquid waste collector. Standard negative pressure rates range between −50 mmHg and −125 mmHg (Ubbink 2008; Vikatmaa 2008).
Risk ratio (RR)	The risk ratio, or relative risk (RR) is the probability that a member of a group who is exposed to an intervention will develop an event relative to the probability that a member of an unexposed group will develop that same event.

Appendix 2. Search strategies

Cochrane Wounds Specialised Register

1 MESH DESCRIPTOR Negative-Pressure Wound Therapy EXPLODE ALL AND INREGISTER

2 MESH DESCRIPTOR Suction EXPLODE ALL AND INREGISTER

3 MESH DESCRIPTOR Vacuum EXPLODE ALL AND INREGISTER

4 'negative pressure' or negative-pressure or TNP or NWPT or NPWT AND INREGISTER 1

5 (sub-atmospheric or subatmospheric) AND INREGISTER

6 ((seal* next surface*) or (seal* next aspirat*)) AND INREGISTER

7 (wound near3 suction*) AND INREGISTER

8 (wound near3 drainage) AND INREGISTER

9 ((foam next suction) or (suction next dressing*)) AND INREGISTER

10 ((vacuum next therapy) or (vacuum next dressing*) or (vacuum next seal*) or (vacuum next assist*) or (vacuum near closure) or (vacuum next compression) or (vacuum next pack*) or (vacuum next drainage) or VAC) AND INREGISTER

11 ('vacuum-assisted') AND INREGISTER

12 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11

13 MESH DESCRIPTOR Surgical Wound Infection EXPLODE ALL AND INREGISTER

14 MESH DESCRIPTOR Surgical Wound Dehiscence EXPLODE ALL AND INREGISTER

15 surg* near5 infect* AND INREGISTER

16 surg* near5 wound* AND INREGISTER

17 surg* near5 site* AND INREGISTER

18 surg* near5 incision* AND INREGISTER

19 surg* near5 dehisc* AND INREGISTER

20 wound* near5 dehisc* AND INREGISTER 456

21 #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20

22 #12 AND #21

The Cochrane Central Register of Controlled Clinical Trials (CENTRAL)

#1 MeSH descriptor: [Negative-Pressure Wound Therapy] explode all trees

#2 MeSH descriptor: [Suction] explode all trees

#3 MeSH descriptor: [Vacuum] explode all trees

#4 ('negative pressure' or negative-pressure or TNP or NWPT or NPWT):ti,ab,kw

#5 (sub-atmospheric or subatmospheric):ti,ab,kw

#6 ((seal* next surface*) or (seal* next aspirat*)):ti,ab,kw

#7 (wound near/3 suction*):ti,ab,kw

#8 (wound near/3 drainage):ti,ab,kw

#9 ((foam next suction) or (suction next dressing*)):ti,ab,kw

#10 ((vacuum next therapy) or (vacuum next dressing*) or (vacuum next seal*) or (vacuum next assist*) or (vacuum near closure) or (vacuum next compression) or (vacuum next pack*) or (vacuum next drainage) or VAC):ti,ab,kw

#11 ('vacuum-assisted'):ti,ab,kw

#12 (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11)

#13 MeSH descriptor: [Surgical Wound Infection] explode all trees

#14 MeSH descriptor: [Surgical Wound Dehiscence] explode all trees

#15 surg* near/5 infect*:ti,ab,kw

#16 surg* near/5 wound*:ti,ab,kw

#17 surg* near/5 site*:ti,ab,kw

#18 surg* near/5 incision*:ti,ab,kw

#19 surg* near/5 dehisc*:ti,ab,kw

#20 wound* near/5 dehisc*:ti,ab,kw

#21 #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20

#22 #12 and #21

Ovid MEDLINE (RCT)

1 exp Negative-Pressure Wound Therapy/

2 exp Suction/

3 exp Vacuum/

4 (negative pressure or negative-pressure or TNP or NPWT or NWPT).tw.

5 (sub-atmospheric or subatmospheric).tw.

6 ((seal* adj surface*) or (seal* adj aspirat*)).tw.

7 (wound adj2 suction*).tw.

8 (wound adj5 drainage).tw.

9 ((foam adj suction) or (suction adj dressing*)).tw.

10 vacuum-assisted.tw.

11 ((vacuum adj therapy) or (vacuum adj dressing*) or (vacuum adj seal*) or (vacuum adj closure) or (vacuum adj assist*) or (vacuum adj compression) or (vacuum adj pack*) or (vacuum adj drainage) or (suction* adj drainage) or VAC).tw.

12 or/1-11

13 exp Surgical Wound Infection/

14 exp Surgical Wound Dehiscence/

15 (surg* adj5 infect*).tw.

16 (surg* adj5 wound*).tw.

17 (surg* adj5 site*).tw.

18 (surg* adj5 incision*).tw.

19 (surg* adj5 dehisc*).tw.

20 (wound* adj5 dehisc*).tw.

21 (wound* adj5 dehisc*).tw.

22 or/13-21

23 12 and 22

24 randomized controlled trial.pt.

25 controlled clinical trial.pt.

26 randomi?ed.ab.

27 placebo.ab.

28 clinical trials as topic.sh.

29 randomly.ab.

30 trial.ti.

31 or/24-30

32 exp animals/ not humans.sh.

33 31 not 32

34 23 and 33

Ovid MEDLINE (economic)

1 exp Negative-Pressure Wound Therapy/

2 exp Suction/

3 exp Vacuum/

4 (negative pressure or negative-pressure or TNP or NPWT or NWPT).tw.

5 (sub-atmospheric or subatmospheric).tw.

6 ((seal* adj surface*) or (seal* adj aspirat*)).tw.

7 (wound adj2 suction*).tw.

8 (wound adj5 drainage).tw.

9 ((foam adj suction) or (suction adj dressing*)).tw.

10 vacuum-assisted.tw.

11 ((vacuum adj therapy) or (vacuum adj dressing*) or (vacuum adj assist*) or (vacuum adj seal*) or (vacuum adj closure) or (vacuum adj compression) or (vacuum adj pack*) or (vacuum adj drainage) or (suction* adj drainage) or VAC).tw.

12 or/1-11

13 exp Surgical Wound Infection/

14 exp Surgical Wound Dehiscence/

15 (surg* adj5 infect*).tw.

16 (surg* adj5 wound*).tw.

17 (surg* adj5 site*).tw.

18 (surg* adj5 incision*).tw.

19 (surg* adj5 dehisc*).tw.

20 (wound* adj5 dehisc*).tw.

21 (wound* adj5 dehisc*).tw.

22 or/13-21

23 12 and 22

24 economics/

25 exp 'costs and cost analysis'/

26 economics, dental/

27 exp 'economics, hospital'/

28 economics, medical/

29 economics, nursing/

30 economics, pharmaceutical/

31 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic*).ti,ab.

32 (expenditure* not energy).ti,ab.

33 value for money.ti,ab.

34 budget*.ti,ab.

35 or/24-34

36 ((energy or oxygen) adj cost).ti,ab.

37 (metabolic adj cost).ti,ab.

38 ((energy or oxygen) adj expenditure).ti,ab.

39 or/36-38

40 35 not 39

41 letter.pt.

42 editorial.pt.

43 historical article.pt.

44 or/41-43

45 40 not 44

46 Animals/

47 Humans/

48 46 not (46 and 47)

49 45 not 48

50 23 and 49

Ovid Embase (RCT)

1 exp suction drainage/

2 exp vacuum assisted closure/

3 (negative pressure or negative-pressure or TNP or NPWT or NWPT).tw.

4 (sub-atmospheric or subatmospheric).tw.

5 ((seal* adj surface*) or (seal* adj aspirat*)).tw.

6 (wound adj2 suction*).tw.

7 (wound adj5 drainage).tw.

8 ((foam adj suction) or (suction adj dressing*)).tw.

9 vacuum-assisted.tw.

10 ((vacuum adj therapy) or (vacuum adj dressing*) or (vacuum adj seal*) or (vacuum adj assist*) or (vacuum adj closure) or (vacuum adj compression) or (vacuum adj pack*) or (vacuum adj drainage) or (suction* adj drainage) or VAC).tw.

11 or/1-10

12 exp Surgical Wound Infection/

13 exp Surgical Wound Dehiscence/

14 (surg* adj5 infection*).tw.

15 (surg* adj5 wound*).tw.

16 (surg* adj5 site*).tw.

17 (surg* adj5 incision*).tw.

18 (surg* adj5 dehisc*).tw.

19 (wound* adj5 dehisc*).tw.

20 or/12-19

21 11 and 20

22 Randomized controlled trials/

23 Single-Blind Method/

24 Double-Blind Method/

25 Crossover Procedure/

26 (random* or factorial* or crossover* or cross over* or cross-over* or placebo* or assign* or allocat* or volunteer*).ti,ab.

27 (doubl* adj blind*).ti,ab.

28 (singl* adj blind*).ti,ab.

29 or/22-28

30 exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/

31 human/ or human cell/

32 and/30-31

33 30 not 32

34 29 not 33

35 21 and 34

Ovid Embase (economic)

1 exp suction drainage/

2 exp vacuum assisted closure/

3 (negative pressure or negative-pressure or TNP or NPWT or NWPT).tw.

4 (sub-atmospheric or subatmospheric).tw.

5 ((seal* adj surface*) or (seal* adj aspirat*)).tw.

6 (wound adj2 suction*).tw.

7 (wound adj5 drainage).tw.

8 ((foam adj suction) or (suction adj dressing*)).tw.

9 vacuum-assisted.tw.

10 ((vacuum adj therapy) or (vacuum adj dressing*) or (vacuum adj seal*) or (vacuum adj assist*) or (vacuum adj closure) or (vacuum adj compression) or (vacuum adj pack*) or (vacuum adj drainage) or (suction* adj drainage) or VAC).tw.

11 or/1-10

12 exp Surgical Wound Infection/

13 exp Surgical Wound Dehiscence/

14 (surg* adj5 infection*).tw.

15 (surg* adj5 wound*).tw.

16 (surg* adj5 site*).tw.

17 (surg* adj5 incision*).tw.

18 (surg* adj5 dehisc*).tw.

19 (wound* adj5 dehisc*).tw.

20 or/12-19

21 11 and 20

22 health-economics/

23 exp economic-evaluation/

24 exp health-care-cost/

25 exp pharmacoeconomics/

26 or/22-25

27 (econom* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic*).ti,ab.

28 (expenditure* not energy).ti,ab.

29 (value adj2 money).ti,ab.

30 budget*.ti,ab.

31 or/27-30

32 26 or 31

33 letter.pt.

34 editorial.pt.

35 note.pt.

36 or/33-35

37 32 not 36

38 (metabolic adj cost).ti,ab.

39 ((energy or oxygen) adj cost).ti,ab.

40 ((energy or oxygen) adj expenditure).ti,ab.

41 or/38-40

42 37 not 41

43 exp animal/

44 exp animal-experiment/

45 nonhuman/

46 (rat or rats or mouse or mice or hamster or hamsters or animal or animals or dog or dogs or cat or cats or bovine or sheep).ti,ab,sh.

47 or/43-46

48 exp human/

49 exp human-experiment/

50 or/48-49

51 47 not (47 and 50)

52 42 not 51

53 21 and 52

EBSCO CINAHL Plus RCT

S37 S23 AND S36

S36 S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35

S35 TI allocat* random* or AB allocat* random*

S34 MH 'Quantitative Studies'

S33 TI placebo* or AB placebo*

S32 MH 'Placebos'

S31 TI random* allocat* or AB random* allocat*

S30 MH 'Random Assignment'

S29 TI randomi?ed control* trial* or AB randomi?ed control* trial*

S28 AB (singl* or doubl* or trebl* or tripl*) and AB (blind* or mask*)

S27 TI (singl* or doubl* or trebl* or tripl*) and TI (blind* or mask*)

S26 TI clinic* N1 trial* or AB clinic* N1 trial*

S25 PT Clinical trial

S24 MH 'Clinical Trials+'

S23 S12 AND S22

S22 S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21

S21 TI (wound* N5 dehisc*) OR AB (wound* N5 dehisc*)

S20 TI (surg* N5 dehisc*) OR AB (surg* N5 dehisc*)

S19 TI (surg* N5 incision*) OR AB (surg* N5 incision*)

S18 TI (surg* N5 site*) OR AB (surg* N5 site*)

S17 TI (surg* N5 wound*) OR AB (surg* N5 wound*)

S16 TI (surg* N5 infection*) OR AB (surg* N5 infection*)

S15 (MH 'Surgical Wound Dehiscence')

S14 (MH 'Surgical Wound Dehiscence')

S13 (MH 'Surgical Wound Infection')

S12 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11

S11 TI (foam suction or suction dressing* or suction drainage) OR AB (foam suction or suction dressing* or suction drainage)

S10 TI vacuum-assisted OR AB vacuum-assisted

S9 TI (vacuum therapy or vacuum dressing* or vacuum seal* or vacuum closure or vacuum compression or vacuum pack or vacuum drainage or vacuum assisted or VAC) OR AB (vacuum therapy or vacuum dressing* or vacuum seal* or vacuum closure or vacuum compression or vacuum pack or vacuum drainage or vacuum assisted or VAC)

S8 TI (wound N5 drainage) OR AB (wound N5 drainage)

S7 TI (wound N5 suction*) OR AB (wound N5 suction*)

S6 TI ((seal* N1 surface* or seal* N1 aspirat*)) OR AB ((seal* N1 surface* or seal* N1 aspirat*))

S5 TI (sub-atmospheric or subatmospheric) OR AB (sub-atmospheric or subatmospheric)

S4 TI (negative pressure or negative-pressure or TNP or NPWT or NWPT) OR AB (negative pressure or negative-pressure or TNP or NPWT or NWPT)

S3 (MH 'Negative Pressure Wound Therapy')

S2 (MH 'Vacuum')

S1 (MH 'Suction+')

EBSCO CINAHL Plus EE

S46 S23 AND S45

S45 S41 NOT S44

S44 S19 NOT (S19 AND S43)

S43 MH 'Human'

S42 MH 'Animal Studies'

S41 S36 NOT S40

S40 S37 or S38 or S39

S39 PT commentary

S38 PT letter

S37 PT editorial

S36 S34 OR S35

S35 TI (cost or costs or economic* or pharmacoeconomic* or price* or pricing*) OR AB (cost or costs or economic* or pharmacoeconomic* or price* or pricing*)

S34 S30 OR S33

S33 S31 OR S32

S32 MH 'Health Resource Utilization'

S31 MH 'Health Resource Allocation'

S30 S24 NOT S29

S29 S25 OR S26 or S27 OR S28

S28 MH 'Business+'

S27 MH 'Financing, Organized+'

S26 MH 'Financial Support+'

S25 MH 'Financial Management+'

S24 MH 'Economics+'

S23 S12 AND S22

S22 S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21

S21 TI (wound* N5 dehisc*) OR AB (wound* N5 dehisc*)

S20 TI (surg* N5 dehisc*) OR AB (surg* N5 dehisc*)

S19 TI (surg* N5 incision*) OR AB (surg* N5 incision*)

S18 TI (surg* N5 site*) OR AB (surg* N5 site*)

S17 TI (surg* N5 wound*) OR AB (surg* N5 wound*)

S16 TI (surg* N5 infection*) OR AB (surg* N5 infection*)

S15 (MH 'Surgical Wound Dehiscence')

S14 (MH 'Surgical Wound Dehiscence')

S13 (MH 'Surgical Wound Infection')

S12 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11

S11 TI (foam suction or suction dressing* or suction drainage) OR AB (foam suction or suction dressing* or suction drainage)

S10 TI vacuum-assisted OR AB vacuum-assisted

S9 TI (vacuum therapy or vacuum dressing* or vacuum seal* or vacuum closure or vacuum compression or vacuum pack or vacuum drainage or vacuum assisted or VAC) OR AB (vacuum therapy or vacuum dressing* or vacuum seal* or vacuum closure or vacuum compression or vacuum pack or vacuum drainage or vacuum assisted or VAC)

S8 TI (wound N5 drainage) OR AB (wound N5 drainage)

S7 TI (wound N5 suction*) OR AB (wound N5 suction*)

S6 TI ((seal* N1 surface* or seal* N1 aspirat*)) OR AB ((seal* N1 surface* or seal* N1 aspirat*))

S5 TI (sub-atmospheric or subatmospheric) OR AB (sub-atmospheric or subatmospheric)

S4 TI (negative pressure or negative-pressure or TNP or NPWT or NWPT) OR AB (negative pressure or negative-pressure or TNP or NPWT or NWPT)

S3 (MH 'Negative Pressure Wound Therapy')

S2 (MH 'Vacuum')

S1 (MH 'Suction+')

Clinical trials registries

We searched each of the following clinical trial registries using the terms ['negative pressure' OR 'vacuum assisted closure' OR 'NPWT' OR 'VAC' AND 'surgical site infection']. We chose the study type' 'interventional studies'; we sought studies with and without results but excluded open studies.

US National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov) (n = 298)

World Health Organization International Clinical Trials Registry Platform (n = 12)

EU Clinical Trials Register (n = 3)

Australian and New Zealand Clinical Trials Registry (n = 30)

Appendix 3. 'Risk of bias' criteria

1. Was the allocation sequence randomly generated?

Low risk of bias

The investigators describe a random component in the sequence generation process such as: referring to a random number table; using a computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots.

High risk of bias

The investigators describe a non-random component in the sequence generation process. Usually, the description would involve some systematic, non-random approach, for example: sequence generated by odd or even date of birth; sequence generated by some rule based on date (or day) of admission; sequence generated by some rule based on hospital or clinic record number.

Unclear

Insufficient information about the sequence generation process is provided to permit judgement of low or high risk of bias.

2. Was the treatment allocation adequately concealed?

Low risk of bias

Participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: central allocation (including telephone, web-based, and pharmacy-controlled randomisation); sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes.

High risk of bias

Participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on: using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or nonopaque or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure.

Unclear

Insufficient information to permit judgement of low or high risk of bias. This is usually the case if the method of concealment is not described or not described in sufficient detail to permit a definitive judgement, for example if the use of assignment envelopes is described, but it remains unclear whether envelopes were sequentially numbered, opaque, and sealed.

3. Blinding - was knowledge of the allocated interventions adequately prevented during the study?

Low risk of bias

Any one of the following.

- No blinding, but the review authors judge that the outcome and the outcome measurement are not likely to be influenced by lack of blinding.
- Blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken.
- Either participants or some key study personnel were not blinded, but outcome assessment was blinded, and the non-blinding of others was unlikely to introduce bias.

High risk of bias

Any one of the following.

- No blinding or incomplete blinding, and the outcome or outcome measurement is likely to be influenced by lack of blinding.
- Blinding of key study participants and personnel attempted, but it is likely that the blinding could have been broken.
- Either participants or some key study personnel were not blinded, and the non-blinding of others was likely to introduce bias.

Unclear

Either of the following.

- Insufficient information is provided to permit judgement of low or high risk of bias.
- The study did not address this outcome.

4. Were incomplete outcome data adequately addressed?

Low risk of bias

Any one of the following.

- No missing outcome data.
- Reasons for missing outcome data are unlikely to be related to true outcome (for survival data, censoring is unlikely to be introducing bias).
- Missing outcome data are balanced in numbers across intervention groups, with similar reasons for missing data across groups.
- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk is not enough to have a clinically relevant impact on the intervention effect estimate.
- For continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes is not enough to have a clinically relevant impact on observed effect size.
- Missing data have been imputed using appropriate methods.

High risk of bias

Any one of the following.

- Reason for missing outcome data is likely to be related to true outcome, with either an imbalance in numbers or reasons for missing data across intervention groups.
- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk is enough to induce clinically relevant bias in intervention effect estimate.
- For continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes is enough to induce clinically relevant bias in observed effect size.
- 'As-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation.
- Potentially inappropriate application of simple imputation.

Unclear

Either of the following.

- Insufficient reporting of attrition/exclusions to permit judgement of low or high risk of bias (e.g. number randomised not stated, no reasons for missing data provided).
- The study did not address this outcome.

5. Are reports of the study free of the suggestion of selective outcome reporting?

Low risk of bias

Either of the following.

- The study protocol is available and all of the study's prespecified (primary and secondary) outcomes that are of interest in the review have been reported in the prespecified way.
- The study protocol is not available, but it is clear that the published reports include all expected outcomes, including those that were prespecified (convincing text of this nature may be uncommon).

High risk of bias

Any one of the following.

- Not all of the study's prespecified primary outcomes have been reported.
- One or more primary outcomes are reported using measurements, analysis methods, or subsets of the data (e.g. subscales) that were not prespecified.
- One or more reported primary outcomes were not prespecified (unless clear justification for their reporting is provided, such as an unexpected adverse effect).
- One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis.
- The study report fails to include results for a key outcome that would be expected to have been reported for such a study.

Unclear

Insufficient information is provided to permit judgement of low or high risk of bias. It is likely that the majority of studies will fall into this category.

6. Other sources of potential bias

Low risk of bias

The study appears to be free of other sources of bias.

High risk of bias

There is at least one important risk of bias. For example, the study:

- had a potential source of bias related to the specific study design used;
- had extreme baseline imbalance;
- has been claimed to have been fraudulent; or
- had some other problem.

Unclear

There may be a risk of bias, but there is either:

- insufficient information to assess whether an important risk of bias exists; or
- insufficient rationale or evidence that an identified problem will introduce bias.

WHAT'S NEW

Date	Event	Description
1 March 2019	New citation required but conclusions have not changed	Updated. Conclusions unchanged.
1 March 2019	New search has been performed	New search. 25 new studies included. 'Summary of findings' table added. Four new co-authors added, Gill Norman, Zhenmi Liu, Jo Dumville and Laura Chiverton.

HISTORY

Protocol first published: Issue 8, 2011
Review first published: Issue 4, 2012

Date	Event	Description
27 August 2014	New citation required but conclusions have not changed	Four trials added (Crist 2014; Masden 2012; Petkar 2012; Stannard 2012), no change to conclusions.
27 August 2014	New search has been performed	First update, new search
13 November 2013	Amended	Acknowledgement added to the funders.
16 May 2012	Amended	Adjustments to text

CONTRIBUTIONS OF AUTHORS

Joan Webster: conceived the review question; designed and coordinated the review update. Extracted data, undertook quality assessment, and analysed and interpreted data. Performed statistical analysis. Wrote and edited the review. Wrote to study authors, experts, or companies, and performed previous work that was the foundation of the current review. Approved the final review update prior to publication, and is a guarantor of the review update.

Zhenmi Liu: extracted data; undertook quality assessment; contributed to writing or editing the review update; and approved the final review update prior to publication.

Gill Norman: extracted data; checked the quality of data extraction; undertook and checked quality assessment; contributed to writing or editing the review update; advised on the review update; and approved the final review update prior to publication.

Jo Dumville: extracted data; undertook quality assessment; contributed to writing or editing the review update; and approved the final review update prior to publication.

Laura Chiverton: extracted data; undertook quality assessment; contributed to writing or editing the review update; and approved the final review update prior to publication.

Paul Scuffham: extracted data, advised on part of the review update, performed part of writing and editing the review update. Performed previous work that was the foundation of the current review update. Performed economic analysis. Approved the updated review prior to publication.

Monica Stankiewicz: extracted data and checked the quality of data extraction. Checked quality assessment and performed part of data analysis and interpretation. Checked the quality of statistical analysis. Advised on the review update and performed part of writing and editing the update. Approved the final review prior to publication and performed previous work that was the foundation of the current update. Approved the updated review prior to publication.

Wendy Chaboyer: extracted data, advised on the review, and performed part of writing and editing the review update. Performed previous work that was the foundation of the current review. Approved the updated review prior to publication.

Contributions of editorial base

Nicky Cullum (Coordinating Editor): advised on methodology, interpretation, and content; edited and approved the review update prior to publication.

Gill Rizzello (Managing Editor): coordinated the editorial process; advised on interpretation, and content; edited the updated review.

Naomi Shaw (Information Specialist): edited the search methods section and search strategy and ran the search for this update.

Ursula Gonthier (Editorial Assistant): edited the Plain language summary and reference sections for this update.

DECLARATIONS OF INTEREST

Joan Webster: none known.

Zhenmi Liu: my employment at the University of Manchester was supported by a grant from the National Institute for Health Research (NIHR Systematic Review Fellowships).

Gill Norman: my employment at the University of Manchester was funded by the National Institute for Health Research and focused on high-priority Cochrane Reviews in the prevention and treatment of wounds.

Jo Dumville: I received research funding from the NIHR for the production of systematic reviews focusing on high-priority Cochrane reviews in the prevention and treatment of wounds.

Laura Chiverton: my work on this review was supported by the NIHR Manchester Biomedical Research Centre.

Paul Scuffham is the Director of a unit contracted to the Australian Department of Health and Ageing to undertake external evaluations of industry submissions to the Pharmaceutical Benefits Advisory Committee.

Monica Stankiewicz: none known.

Wendy Chaboyer: none known.

SOURCES OF SUPPORT

Internal sources

- Royal Brisbane and Women's Hospital, Australia.

  Time to conduct review
- Griffith University, Australia.

  Time to conduct review

- Division of Nursing, Midwifery and Social Work, School of Health Sciences, Faculty of Biology, Medicine and Health, University of Manchester, UK.

External sources

- The National Institute for Health Research (NIHR), UK.

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- NIHR Manchester Biomedical Research Centre, UK.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Changes in the 2018 update

- We have changed the title and the focus of the review. In the previous two versions, we included studies that investigated skin grafts and also those investigating surgical wounds expected to heal by primary intention. In this version of the review, we did not include studies of skin grafts. This decision was made after consultation with the Editorial base and was based on the following considerations: the healing mechanisms and outcome measures are different for graft sites and incisional wounds, so there was a clear, clinical reason for focusing on one type of wound; we also clarified that trials using NPWT following surgery that involved harvesting veins following flap elevation would also be excluded. Outcomes measures from these trials (such as flap necrosis, lymphorrhagia, and lymphoedema) also differed from primary closure surgery. In addition, the number of trials reporting outcomes following the application of NPWT has been growing exponentially, with the majority of these trials focusing on previously uninvestigated types of surgery using primary closure. Because of this, it seemed timely to focus this review only on 'primary closure' surgery.
- We modified the wording of the title from 'primary intention' to 'primary closure'. The wording change was needed because closure by primary intention would mean the inclusion of grafts and flap surgery trials, whereas primary closure means the surgical edges are approximated and held together with sutures, glue, etc. Primary closure is the simplest closure technique and more accurately reflects the intention of the review.
- We removed the outcome 'graft failure' in line with the new focus of the review.
- We removed the outcome 'time to complete healing', as this outcome was deemed not to be appropriate for surgical wounds expected to heal by primary intention (it is difficult or impossible to determine or define the point of healing for a wound healing in this way). For this reason, 'proportion of surgical wounds healing by primary intention that completely heal' was removed for the first update and 'reoperation' added (see also 'Changes in previous versions' below).
- We added one additional outcome: 'readmission within 30 days for a wound-related complication'. We believe this outcome is important because, while readmission for repeat surgery is one of our current outcomes, the reason for readmission is not always stated in study reports.
- We have split 'adverse events' into 'surgical site infection' and 'dehiscence'.
- We removed the words 'and including utility scores representing health-related quality of life' from the outcome 'healthcare costs' and included it under the outcome 'quality of life'.
- We split one of our secondary outcomes, 'seroma/haematoma', into two separate outcomes. This decision was based on differing definitions and aetiologies of the two conditions. A seroma is a collection of clear, serous fluid, which sometimes collects under a surgical wound, whereas a haematoma is a collection of blood outside a blood vessel.
- We changed the outcome 'fracture blisters' to 'skin blisters', as some blisters are associated with dressings that cover wounds from surgery that is not fracture surgery.
- We have split 'cost' into four separate outcomes: 'dressing-related costs', 'resource use', 'incremental cost per quality-adjusted life year', and 'estimated incremental cost-effectiveness ratio'.

- We have also broken up costs into two categories. The first ('dressing-related costs') is a simple cost comparison from the intervention study reports, and the second ('cost') is a full economic analysis from the two cost-effectiveness studies. This analysis contains three outcomes: resource use, incremental cost per quality-adjusted life year, and estimated incremental cost-effectiveness ratio.
- We have added three additional items of data extraction: 'source of funding', 'prospective registration on a clinical trials registry', and 'economic data (healthcare costs)'. We made these additions to reflect the importance of prospective registration in the assessment of risk of bias in several domains, and in response to the insistence in many quality journals on prospectively registering clinical trials as a quality measure.
- We updated our search strategies, adding new terms for negative pressure wound therapy, and changed the term 'surgical' to 'surgical site infection' in the trial registries' search.
- We included an additional (standard) sensitivity analysis with the following wording: 'We performed a sensitivity analysis on the primary outcomes (surgical site infection) to assess the influence of removing studies classified as being at high risk of bias from the meta-analysis. We excluded studies that were assessed as having high or unclear risk of bias in the key domains of adequate generation of the randomisation sequence, adequate allocation concealment, and blinding of outcome assessor. We planned but were unable to undertake a similar analysis for the outcome of dehiscence.
- We removed allocation concealment and type of randomisation from the sensitivity analyses; they are included in the new sensitivity analyses described above. We removed duration of follow-up from the sensitivity analyses.
- We changed one subgroup analysis from 'type of surgery (traumatic wounds, reconstructive procedures, other post-surgical wounds; skin grafts)' to 'type of surgery' without qualification.
- We removed one comparison (industry funded versus non-industry funded) following advice from the Editorial base. We removed one comparison (one negative pressure closure method compared with another), as the study providing data for this comparison, Dorafshar 2012, has now been excluded in line with the new focus of the review on surgical wounds healing by primary closure only.
- We have updated the methods used to assess heterogeneity and taken this into account in our analyses; we have changed methods of analysis as appropriate to the evidence that is now included in this updated version.
- We used the method for classifying economic evaluation described by Husereau and colleagues (Husereau 2013), rather than the evaluation described by Drummond 2005. This decision was based on the knowledge that the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist has become the standard for economic evaluations. The checklist was developed in collaboration with a range of organisations, and includes Drummond as a co-author.
- We have added a 'Summary of findings' table to the review and used a GRADE assessment of the certainty of the evidence throughout.

Changes to previous versions

We added a comparison (one negative pressure closure method compared with another) to the previous version of this review, but this has now been removed (see comment above).

We expanded the list of extracted data from the protocol to include:

- study dates;
- number of participants per group;
- information about ethics approval, consent, and conflict of interest.

In trials of skin grafts, graft failure is an important outcome. We failed to include this as either a primary or secondary outcome in the protocol for the original review. We also failed to include length of hospital stay, which is important for any economic analysis. Consequently, we included graft failure and length of hospital stay as additional outcomes post hoc.

- In the previous update, we removed the primary outcome 'proportion of surgical wounds healing by primary intention that completely heal (surgical wounds may include split skin grafts, full skin grafts, or any primary wound closure)'. This decision was based on our experience conducting the first version of this review, where we noted that 'it has become clear to us that this outcome is not appropriate for surgery that is expected to heal by primary intention; most clean surgical wounds will completely heal in a relatively short time. Moreover, determining when a surgical incision is 'completely healed' is difficult. Consequently, wound healing should not be included as a primary outcome for future updates'.
- In the first version of the review, we considered any wound complications under the heading 'adverse events'. As many of these 'events' are qualitatively different and of varying levels of importance, we subsequently included only 'surgical site infection' and 'dehiscence' under the heading 'adverse events'. We moved other wound-related outcomes that were previously included under the primary outcome 'adverse events' (such as fracture blisters, seromas, etc.) to the secondary outcomes. We changed 'graft loss' to 'graft failure' and added it as a separate outcome because it is an important outcome for skin graft studies, and in our protocol we did not include any outcomes that were specific to skin grafts. We also added a new secondary outcome, 'reoperation', as this is an important outcome that indicates the severity of any wound dehiscence or graft loss.
- We changed the wording in the sections 'Unit of analysis issues' (we had not anticipated in the original version of the review that multiple wounds might be an issue) and 'Dealing with missing data' (to clarify what we intended to do).

INDEX TERMS

Medical Subject Headings (MeSH)

*Skin Transplantation; *Wound Healing; Bandages; Blister [epidemiology]; Hematoma [epidemiology]; Negative-Pressure Wound Therapy [economics] [instrumentation] [*methods] [mortality]; Orthopedic Procedures; Quality-Adjusted Life Years; Randomized Controlled Trials as Topic; Reoperation [statistics & numerical data]; Seroma [epidemiology]; Surgical Procedures, Operative [mortality]; Surgical Wound Dehiscence [epidemiology] [*prevention & control]; Surgical Wound Infection [epidemiology] [*prevention & control]; Wounds and Injuries [surgery]

MeSH check words

Humans